I. Multidisciplinary beamlines at LNS

II. Radiobiological facility

GAP Cirrone, P Pisciotta,
FP Cammarata, V Marchese, G Petringa, G Russo

Outline

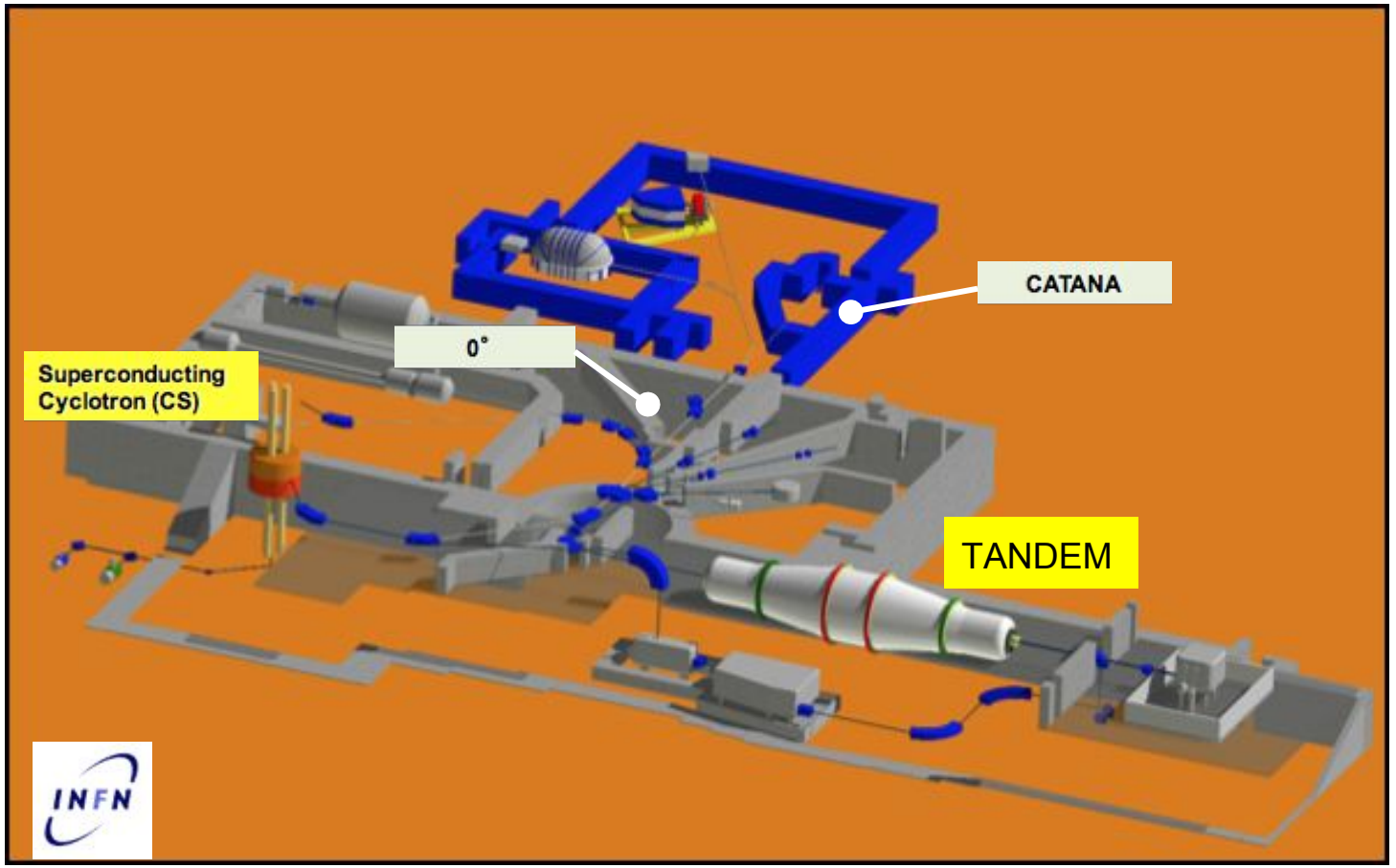
- CATANA protontherapy beamline
- Zero degrees beamline
- Dosimetric and monitoring devices
- Monte Carlo simulations instruments
- Radiobiology facilities
  - Cells growth laboratory
  - In-vitro and in-vivo activities

Multidisciplinary beamlines

Two experimental rooms available for multidisciplinary irradiations

- **CATANA protontherapy** room (clinical and monoenergetic proton beams, 62 MeV)
- **0° beamline** (proton and light ions up to 80 AMeV)

Equipments for beam diagnostic, dosimetry and monitoring are available



CATANA beamline

Dedicated to proton therapy irradiation

Dosimetry and radiobiology

In-air only

Energy passively degraded

Fast and easy positioning system

Double scattering system for lateral spread → homogeneity below 3%

Collimated beams (1-35 mm diameter)

Fixed elements limiting some applications:

- Fluence
- High level homogeneity but no point-like spot like
- Radiation protection issues during the patient treatments may limit beam current

0° beamline

Transported beams: p, He, C, O, Ne, Ar, Kr, Xe, ..

Relative and absolute dosimetry

In-air only but also in-vacuum possibility

Certified beamline for ESA experiment

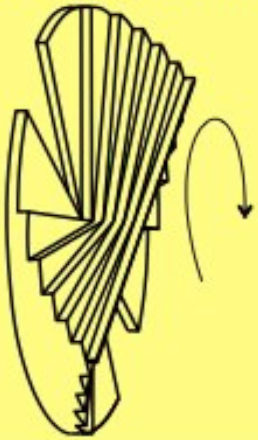
Fast and easy positioning system

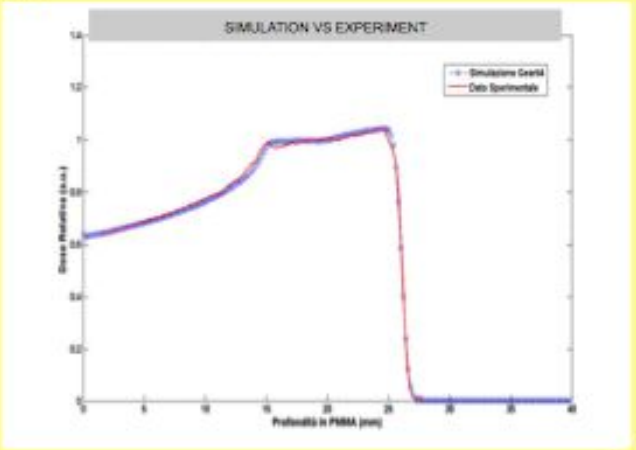
No particular constraints from fixed elements but ...

- Homogeneity about 15%
- Final collimator can be removed but alignment must be repeated (4 h)

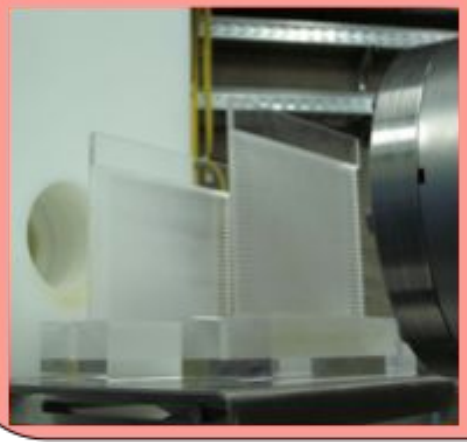
Longitudinal dose distributions

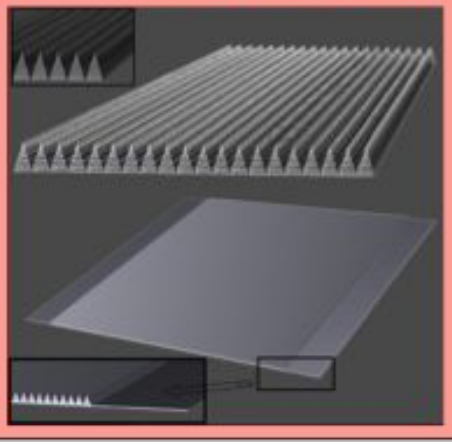
protons at Catana room

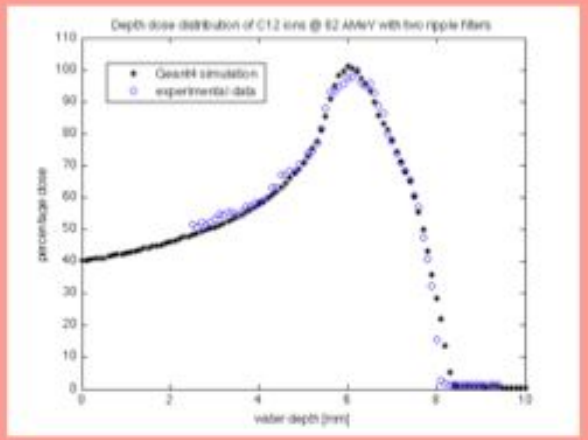




ions at 0° room



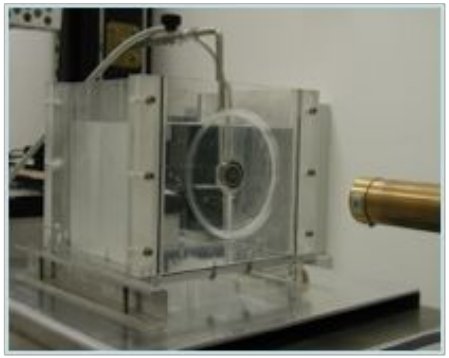




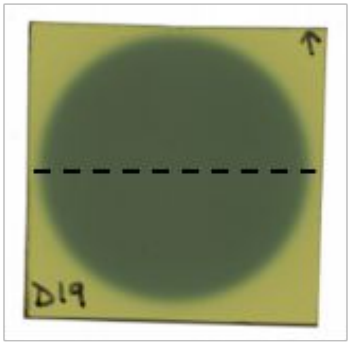
Absolute dosimetry and on-line beam monitoring

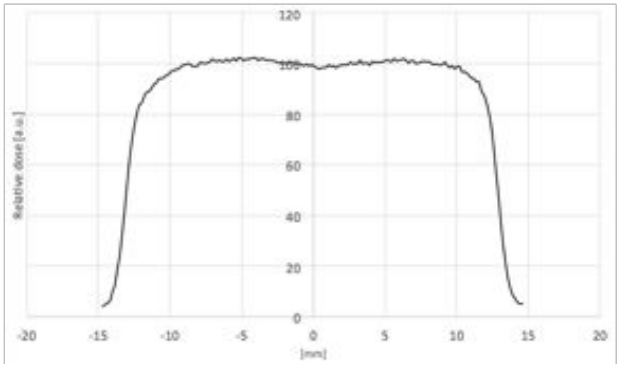
Dose distributions measurements

✓ Reference absolute dosimetry in a water phantom using plane-parallel PTW Markus ionization chamber, calibrated according to IAEA code of practice.

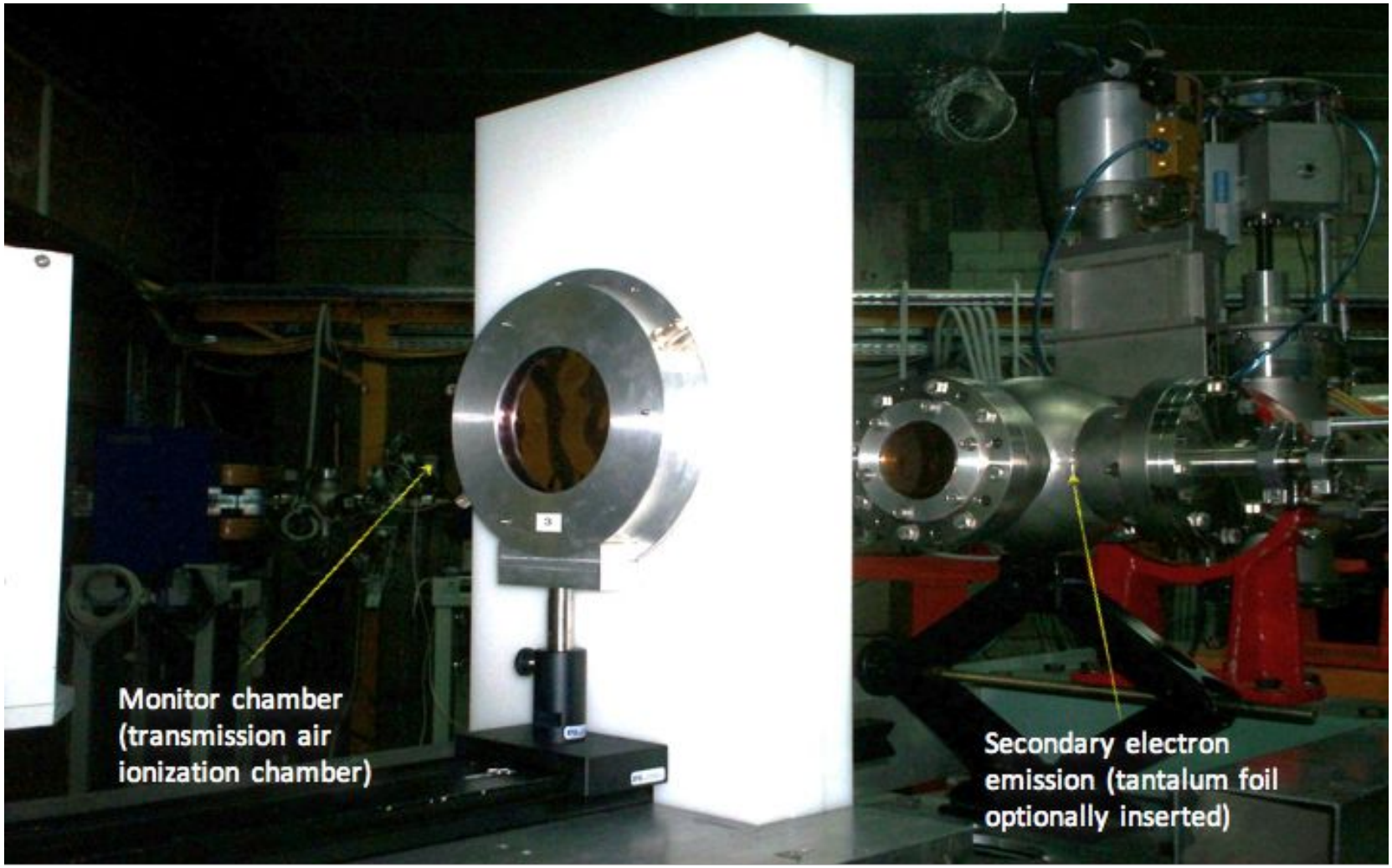


✓ Lateral dose distribution finally checked with radiochromic films (EBT3, HD-V2)



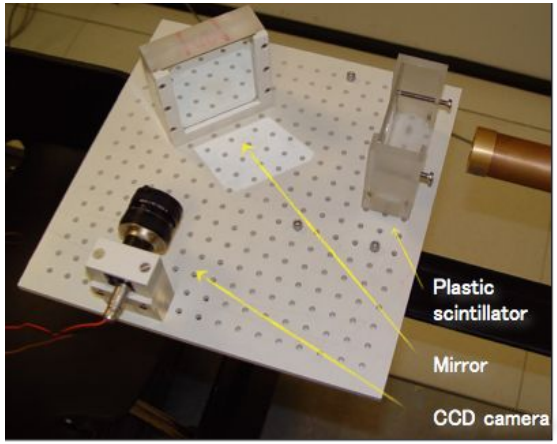


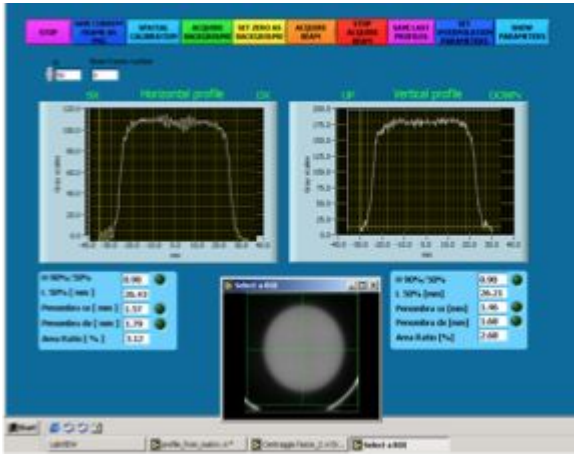
Absolute dosimetry and on-line beam monitoring



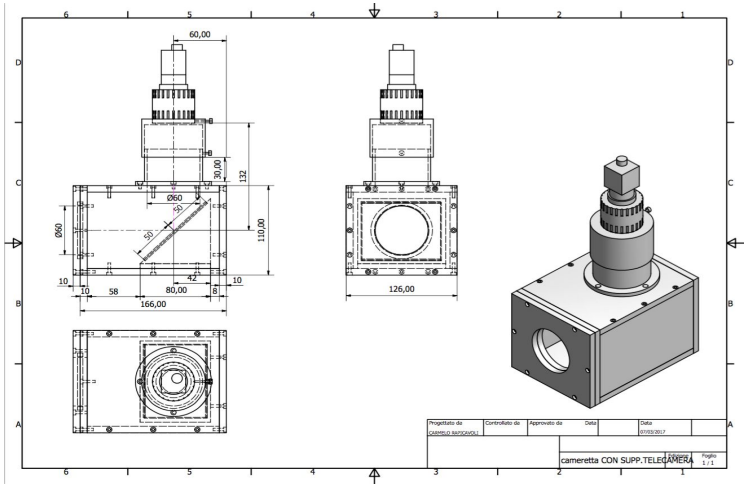
Relative dosimetry: Beam profile monitoring

2004





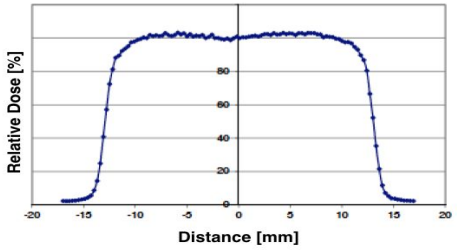
2017 (new set-up)



Plastic Scintillator EJ204: 0.5mm - 1mm

CCD Basler NI supported

Dedicated analysis software

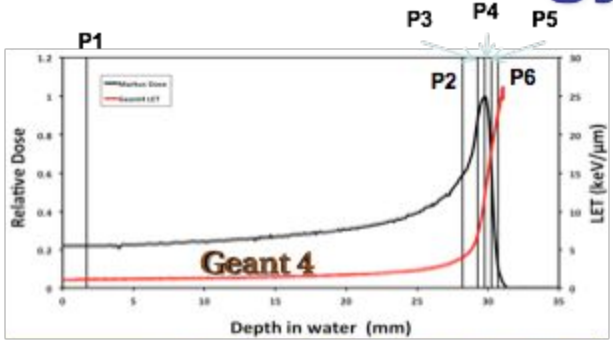


Si.a.tel
sistemi automazione telecontrollo

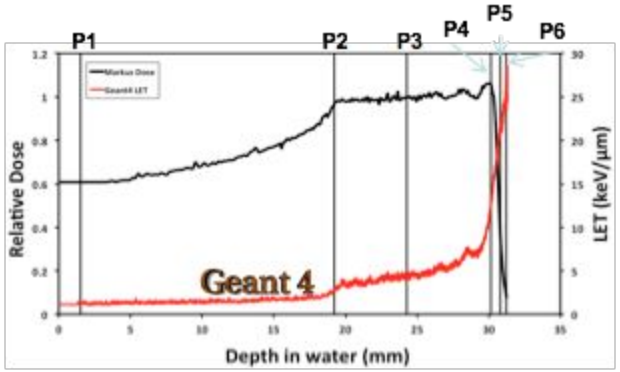
SCIONIX

Radiobiology: cells positioning

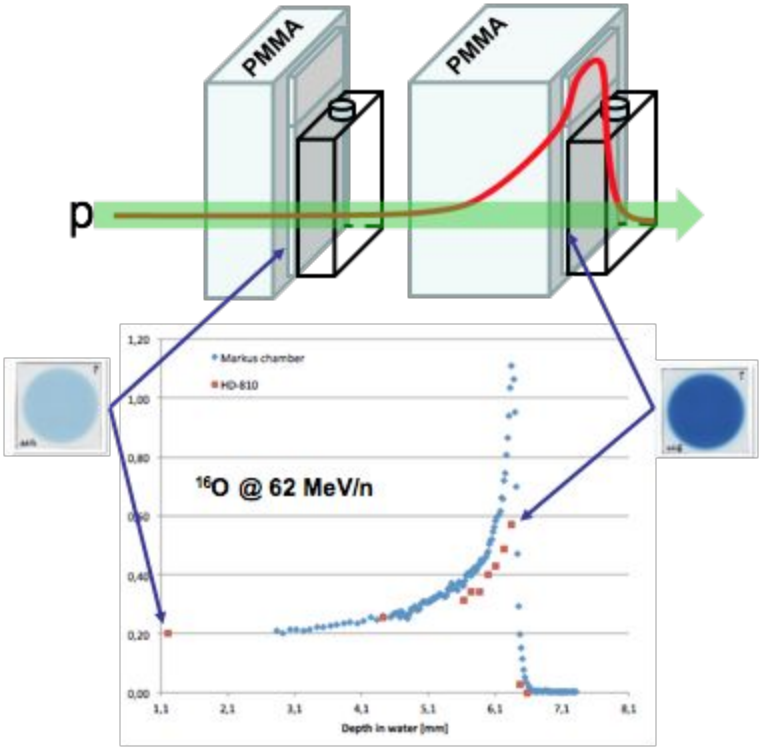
Radiobiology: cell positioning



	P1	P2	P3	P4	P5	P6
Depth water [mm]	1.38	20.23	24.59	27.69	29.48	30.08
LET [keV/µm]	1.2	2.6	4.5	13.4	21.7	25.9



	P1	P2	P3	P4	P5	P6
Depth water [mm]	1.38	27.42	29.21	29.8	30.7	31.29
LET [keV/µm]	1.11	4.0	7.0	11.9	18.0	22.6

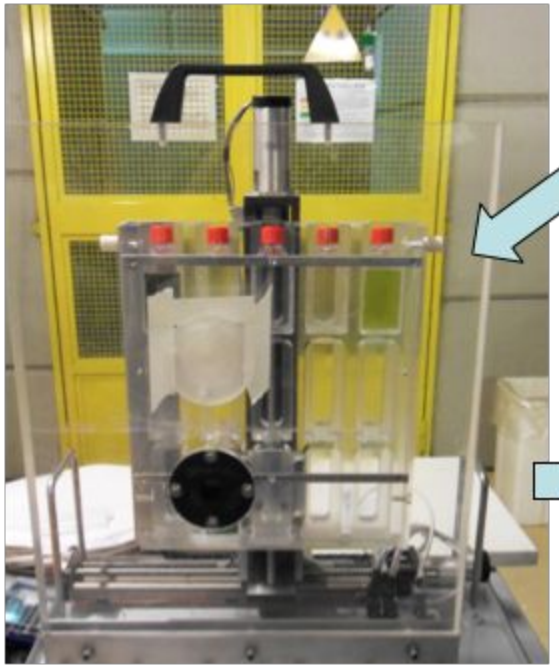


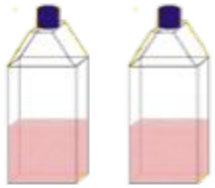
50 µm positioning accuracy achieved combining Gafchromic films with Markus Chamber

Radiobiology: irradiation device

Radiobiology: irradiation device

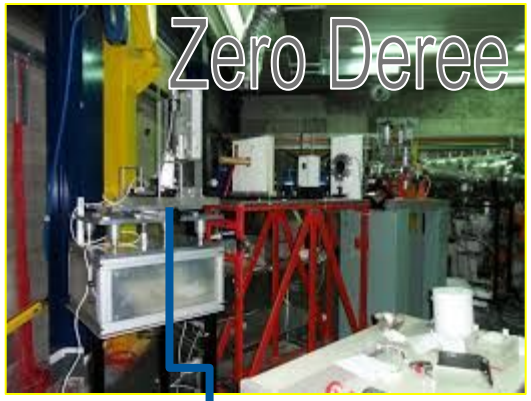
The software for remote cell positioning has been updated



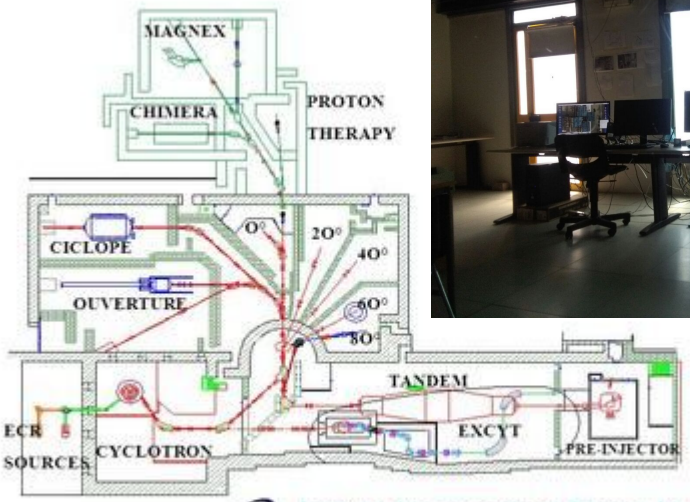


- Motorized system with 100 um precision
- Remotely controlled
- Interfaced with beam control system
- Real time dose-rate monitoring

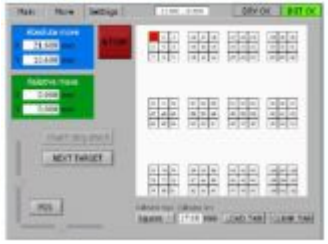
Acquisition room allow the monitoring and controlling of the beam

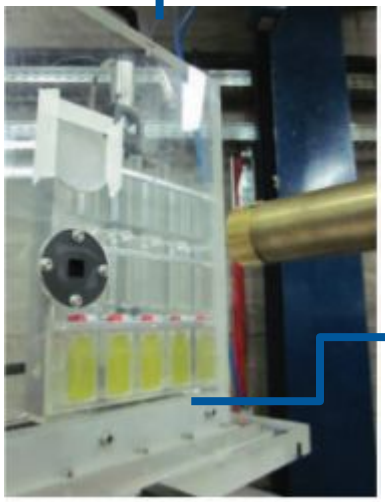


Software control system permit to handle mechatronic to flasks movement

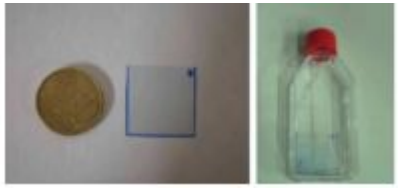


Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali del Sud





A special support located within the irradiation room permit the flasks movement



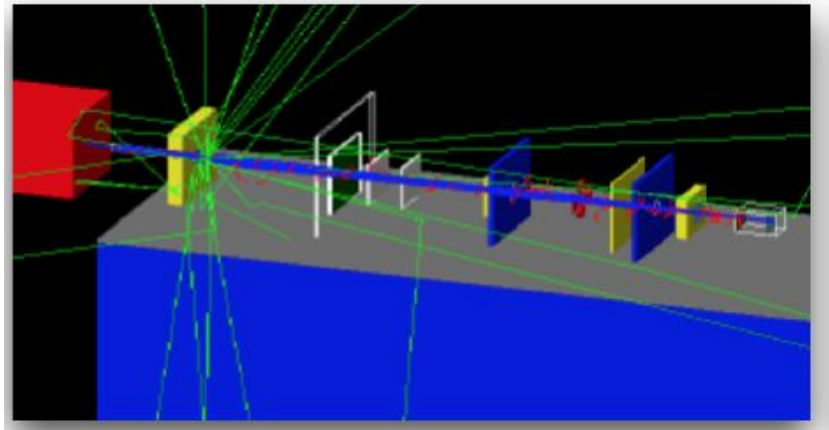
Using gafchromic film is possible to verify the beam uniformity and the geometry of system

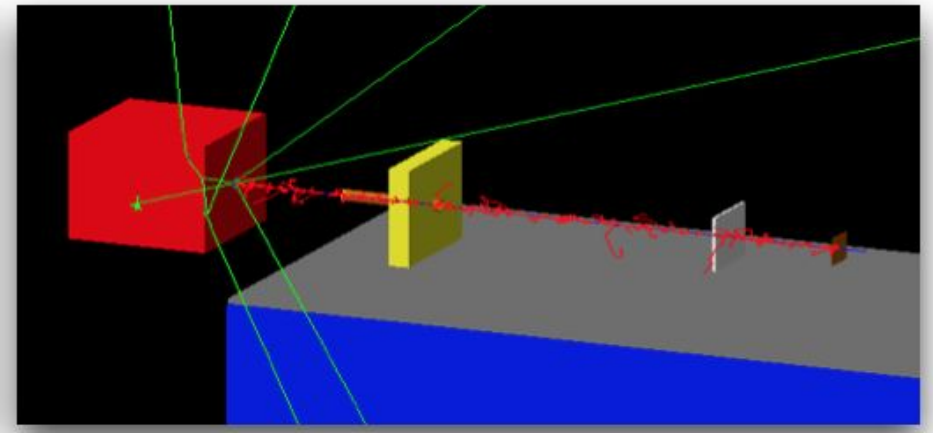
Monte Carlo support with the Geant4 toolkit

Beamline Simulations

CATANA beamline

zero degree beamline





Hadrontherapy example inside the Geant4 distribution simulating the two LNS beam lines

LET calculation

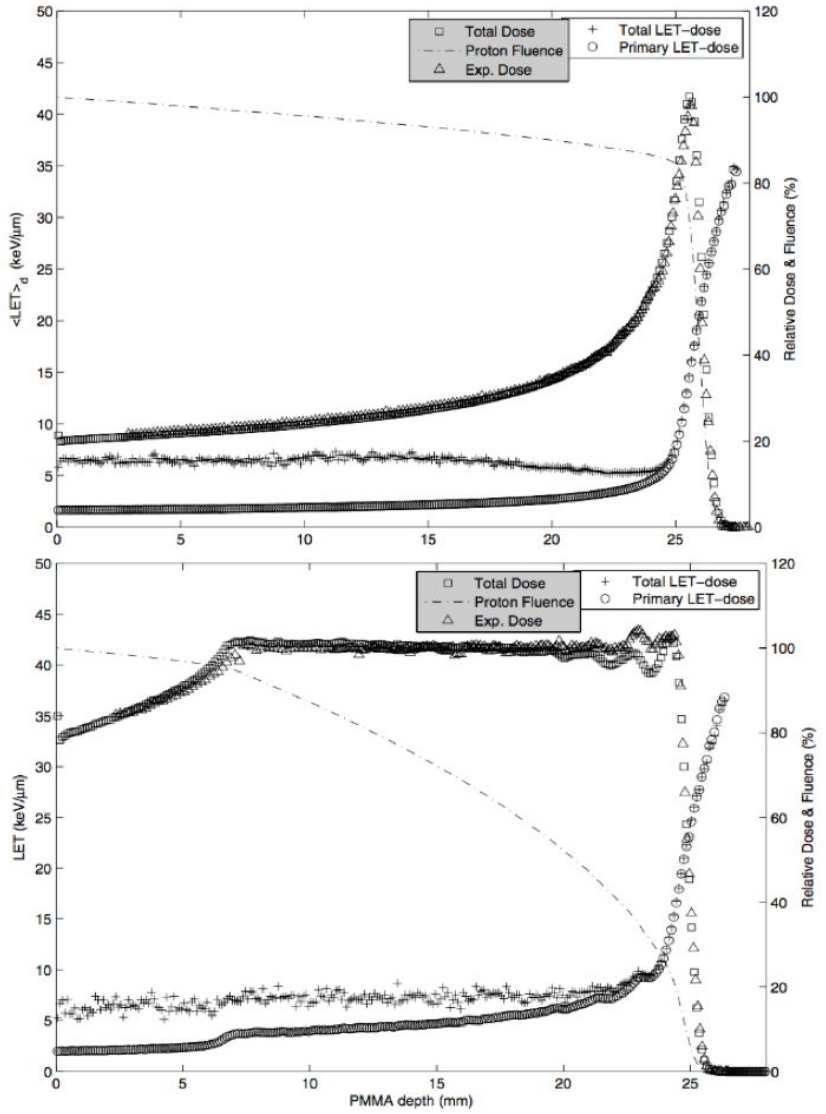
Total Let-dose

Primary LET-dose

$$\bar{L}_d^{MC}(z) = \frac{\Sigma_{k=1}^{M} dE_k (dE_k/dx_k)}{\Sigma_{k=1}^{M} dE_k}$$

step-by-step are retrieved information about:

- Step Length
- Particle type (in term of Z and A)
- Deposited Energy

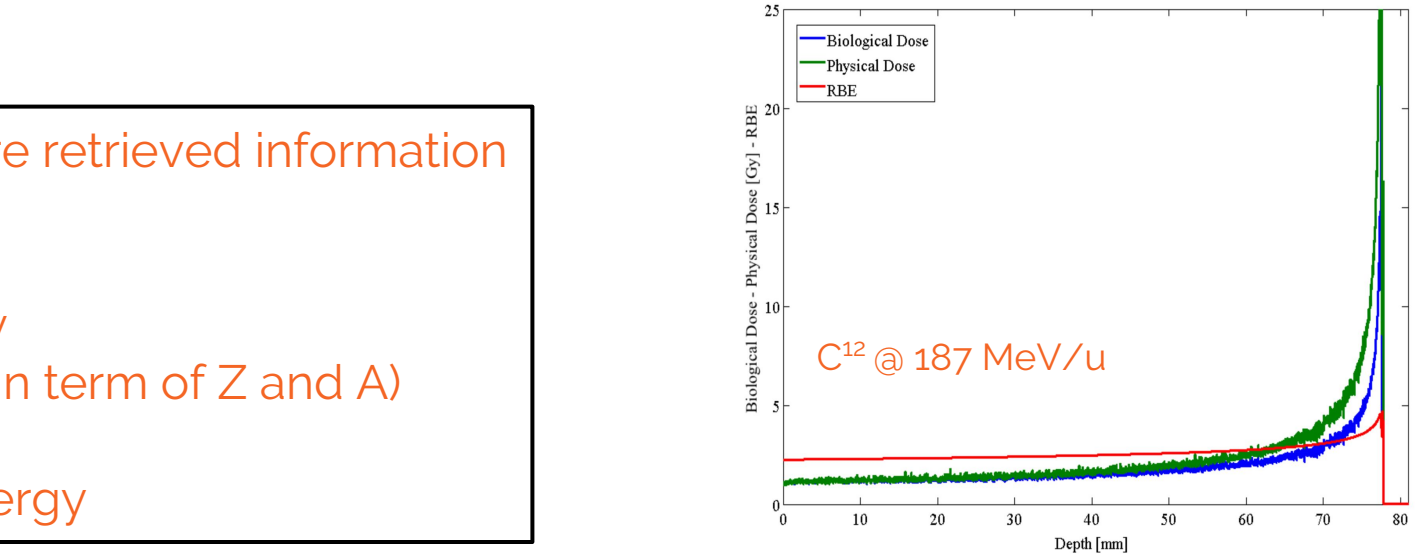


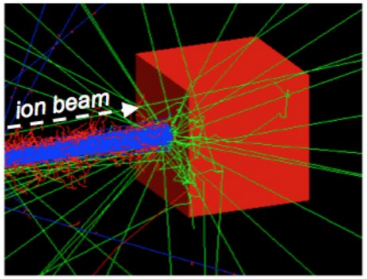
Romano et al. et al. 'A Monte Carlo study for the calculation of the average linear energy transfer (LET) distributions for a clinical proton beam line and a radiobiological carbon ion beam line'Physics in Medicine and Biology 59 (2014)

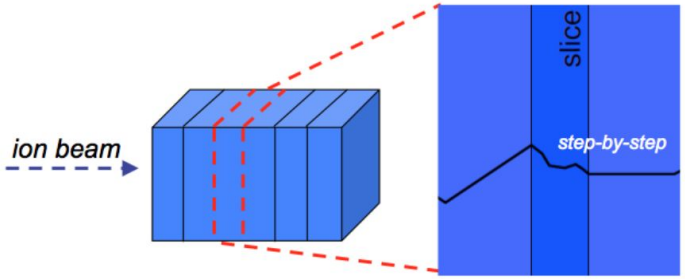
RBE class

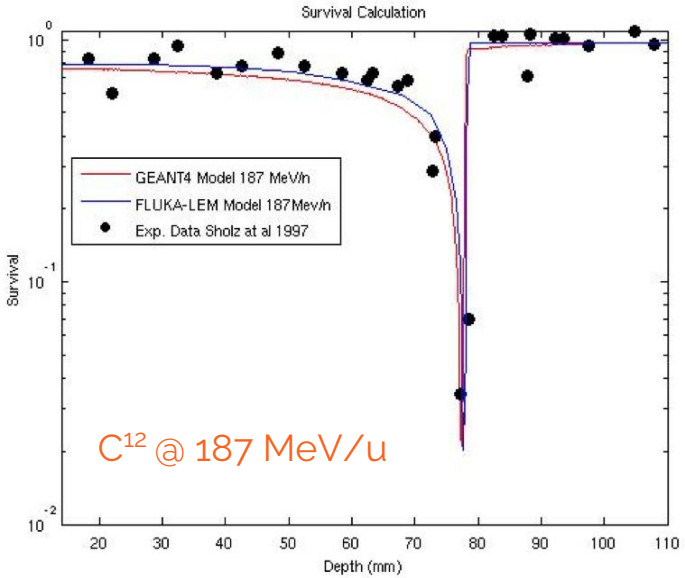
step-by-step are retrieved information about:

- Kinetic energy
- Particle type (in term of Z and A)
- LET
- Deposited Energy









Radiobiology laboratory

Radiobiology: cell growth laboratory

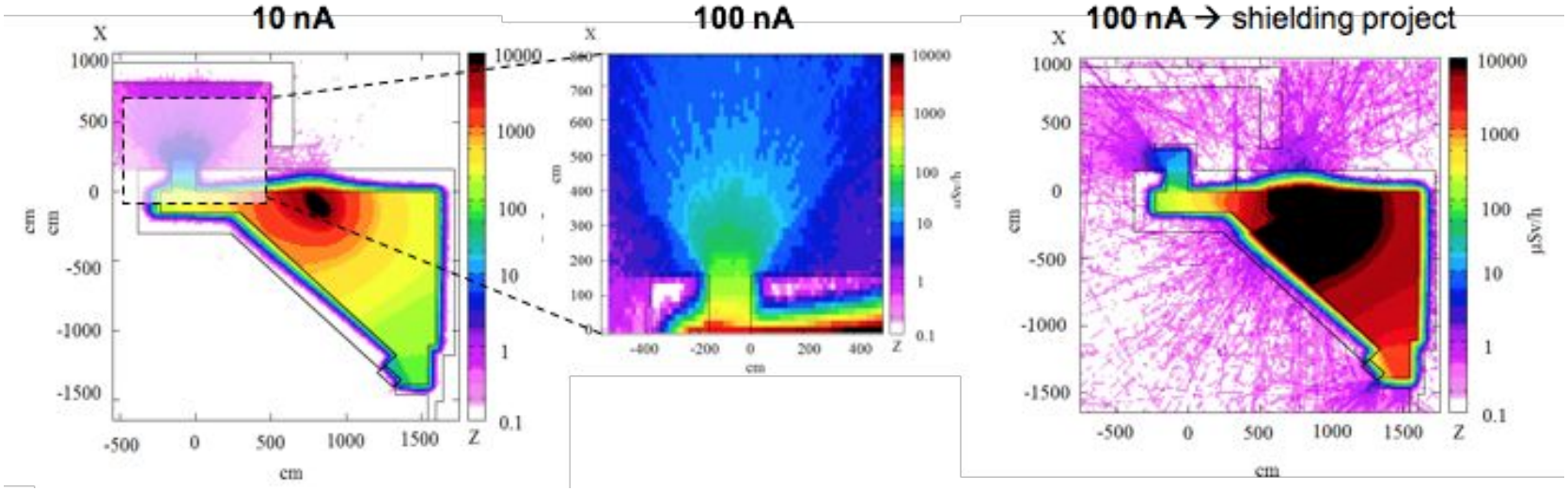
- New laboratory (larger and more equipped than the previous one)
- Fully equipped with the basic system for a biological analysis
  - Centrifuge
  - Incubators
  - Sterilizer
  - Microscope
- CO_2 "centralized" system

Overlapping of several groups no more critical

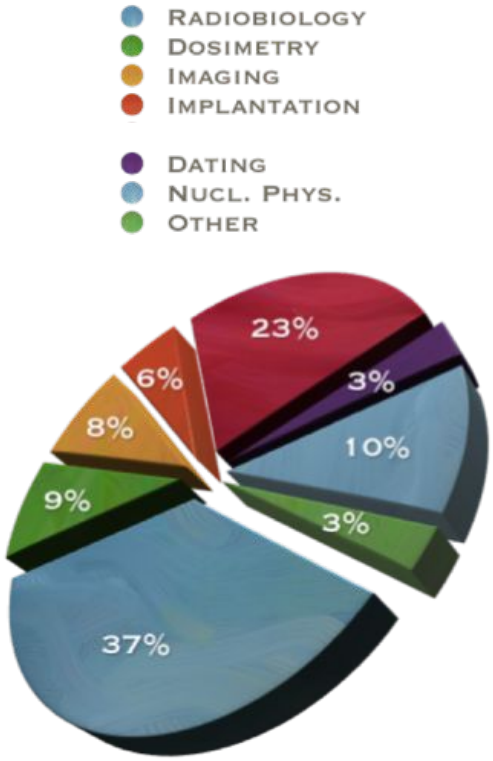
High current irradiations

- Requirements for high currents → **radiation hardness** experiments
- Upgrade for enabling **100 nA** beam current at 0° room (10 nA so far)
  - **DIAPIX** experiment for CVD diamond detectors radiation damage
  - Radioprotection issues → environmental radiation due on neutron production
  - Funds from "Progetto Premiale IRPT " for the realization of new **shielding** solutions
  - Same funds used also for cabling

Monte Carlo calculations of environmental radiation fields with p beams @ 62 MeV in zero degree room (by S. Russo and R. Leanza)



Users' statistics



- Both Catana and zero degree rooms recently used for scheduled experiments
- Dosimetry / beam monitoring / beam shaping / position procedures: tested and well working

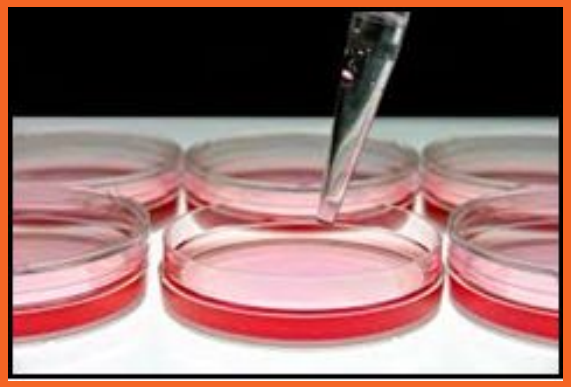
User requirements:

- ☑ Absolute and relative dosimetry
- ☑ On line measurements of beam lateral homogeneity
- ☐ Precise fluence measurements and contamination characterization
- ☑ Accurate protocol for checking the cell sample position
- ☑ Larger spaces for radiobiology and post experiment cell survival analysis
- ☑ High current experiments
- ☑ Cabling connection outside/inside the exp. Room (on-going)

2017

12 Groups for an average of 40 shift

Radiobiology	6 (3 in-vivo)
Detectors	5
Imaging	1



cell biology

II. Radiobiological facility

animal sciences

in collaboration with:

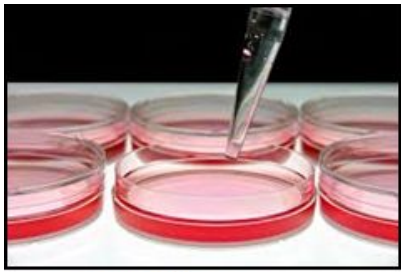
RadioBiological Laboratory

PETs *- Preclinical Hadrontherapy Studies*
MoVe - IT *- Modeling and Verification for Ion beam Treatment planning*

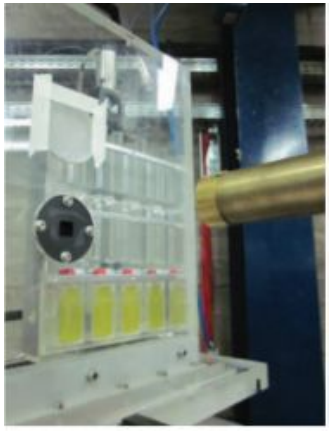
In vitro / ex vivo cell-based models

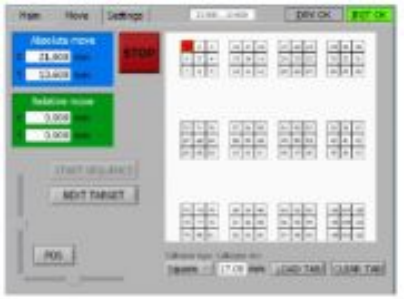
Using different cell lines:

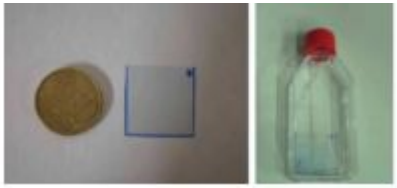
- Tumorigenic: MCF7; MDA-MB-231 (BC cell lines) - U87 (Glioma cells)
- Non-tumorigenic: MCF10A (BC cell lines)
- Normal and tumour primary cells from patients biopsies
- Under study:
  - new drugs and/or molecules radio sensitizing (LDS Siena - Betulla, etc…)



In vitro positioning system







Preclinical Hadrontherapy facilities

PETs *- Preclinical Hadrontherapy Studies*
MoVe - IT *- Modeling and Verification for Ion beam Treatment planning*

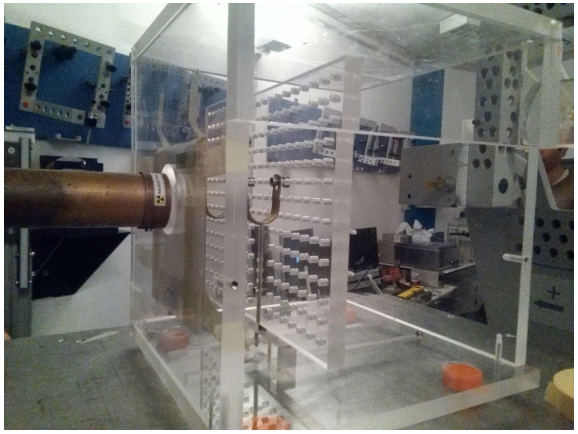
In vivo approach with mouse models

- Animal facility
- Health ministry **authorization**
- **Dosimetry** and **simulation** studies
- **Personnel Felasa cat.C**

Hadrontherapy on tumours inoculated in mice

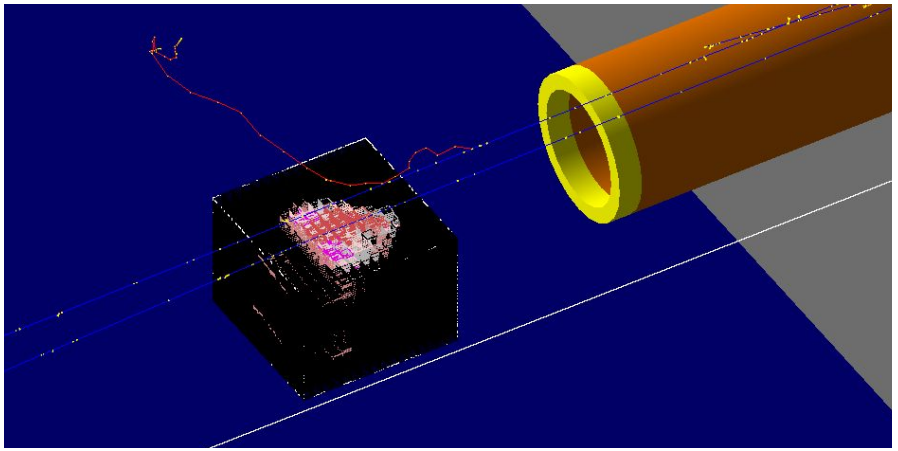
- **RBE** relative biological effectiveness
- intra-tumor heterogeneity.

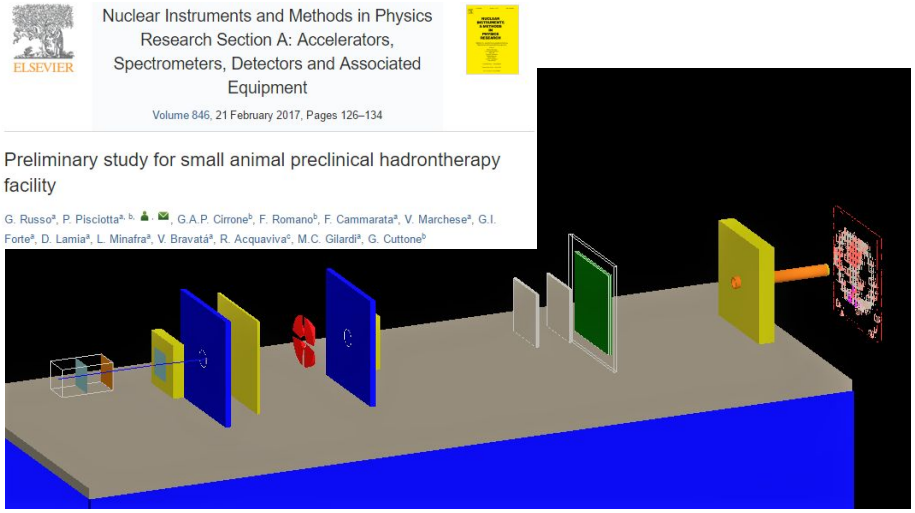
In vivo positioning system



Preclinical Monte Carlo studies

- **State of art**
  - **Validation:**
    - **Experimental validation** using gafchromic films and ionization chamber
  - **Preliminary in vivo test:**
    - Small animal treatment plans. **Dose** distribution and **LET** assessment.





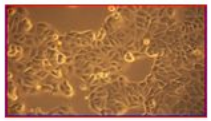
- Reproduces mouse tissue based on **DICOM** micro-CT images
- Reproduces **CATANA beam line**
- Permits to evaluate a **3D dose maps** for different beam configurations (e.g. modulators, range shifters, collimator diameters, etc.)

Biomarkers discovery by proteogenomic technologies

studies performed by

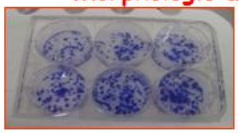
Hadrontherapy

1.*In vitro approach with cell culture models*



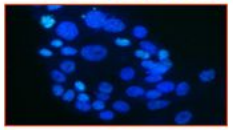
2.*In vivo approach with mouse models*

Morphologic and Clonogenic Assay



Evaluation of morphology and cell viability in terms of reproductive capacity, by clonogenic survival assay of treated cells

Immunofluorescence

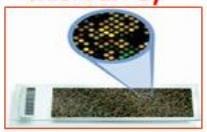


Analysis of γ-H2AX foci formation after treatment, as a marker of sensitive early cell response to the presence of DNA double-strand breaks

Luminex

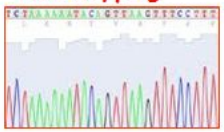
Evaluation of inflammatory response induced by treatment and able to influence cell fate decision

Microarray



Comparative differential gene expression analysis beween treated and untreated cells by Microarray

Genotyping



Analysis of genetic alterations that could regulate radio-sensitivity and cell survival/death balance

New research platform
and
Radiopharmaceutical
production

Already ready!!!

"**CATANA**" Centro di AdroTerapia e Applicazioni Nucleari Avanzate

Proton irradiation of **small animals**

Laboratory Animal Science **FELASA** cat.**C**

Quantification and elaboration of **diagnostics imaging**

"**CAPIR**" Center for Advanced Preclinical in vivo Research **PET facility** (checked in 4th May 2017)
Optical Imaging and **Ultrasound Imaging** facility

"**Behaviour**" platform

Coming soon

Cyclotron and Radiopharmaceuticals production for internal clinical purpose:

[^{18}F]-FDG
[^{11}C]-Colina
[^{11}C]-Metionina
[^{68}Ga]-DOTATOC

Development of innovative radiopharmaceuticals:

[^{18}F]-FLT
[^{18}F]-MISO
[^{18}F]-Fluoruro
[^{18}F]-Colina

Coming soon

Infrastructure update of **RadioBiological Laboratory** & **Preclinical Facilities:**

- **Fluorescence microscopy** (innovative radiobiological biomarker)
- **-80 fridge** and **liquid nitrogen dewar**
- **metabolic cage**

Coming soon

Thanks to

Amico Antonio

Cammarata Francesco

Leanza Renata

Marchese Valentina

Milluzzo Giuliana

Pisciotta Pietro

Petringa Giada

Russo Giorgio

The technical staff of LNS accelerators division


THANK
YOU
GRACIAS
ARIGATO
SHUKURIA
DANKSCHEEN
BÏYAN
SHUKRIA
TINGKI
YAQHANYELAY
TASHAKKUR ATU
SUKSAMA
EKHMET
MEHRBANI
GRAZIE
MAAKE
KOMAPSUMNIIDA
JUSPAXAR
GOZAIMASHITA
EFCHARISTO
PALDIES
BOLZÏN
MERCI