Attività per Life Science della Sezione INFN di Milano con UniMi e PoliMi

Radiobiologia per adroterapia *(D. Bettega et al.)*

Monitoring in tempo reale del range in adroterapia *(G. Battistoni et al.; C. Fiorini et al.)*

Applicazioni medicali del codice Monte Carlo FLUKA *(P. Sala, G. Battistoni et al.)*

Applicazioni di Nuove Tecniche di Accelerazioni di Particelle in Adroterapia *(D. Giove et al.)*

Microdosimetria a stato solido *(S. Agosteo, A. Fazzi et al.)*

Radioisotopi innovative per Teragnostica *(M. Bonardi, F. Groppi, et al.)*

Radiobiology of Combined Chemo-Hadrotherapic Treatments

(D. Bettega, P. Calzolari, M. Lafiandra, INFN & UniMi)

Combined effect of charged particles irradiation and anticancer drugs in cultured tumor cells

(collaboration INFN Mi / UniMi, CNAO, Istituto Tumori Mi)

Combined radiochemotherapy treatment modality:
-to improve locoregional tumour control and to reduce distant failure;
-to reduce the total treatment Dose in radiosensitive patients

In the last years:
-several new drugs (various mechanisms of interaction with radiation)
-many preclinical studies on the combined effect of standard radiotherapy and chemotherapy

but

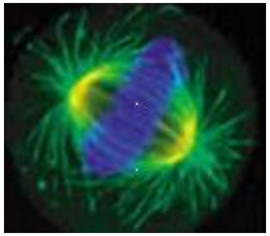
very few data on the interaction of drugs with charged particles irradiation, a very promising treatment for many tumors due to their dosimetric and radiobiological properties.

Epothilone B, Microtubule Stabilizing Agent (MSA) :

Defective mitotic spindle formation, cell cycle arrest in M phase, apoptosis or post mitotic death

Accumulation of cells in the most radiosensitive →

G2-M phase of the cell cycle → Radiosensitizer ??



reduces DNA repair capability of tumor cells

antivascular and antiangiogenic effects

inhibits cell migration

At the present used for chemotherapic treatments : fewer side effects, superior pharmacological and anticancer activity, compared with previous MSA (taxanes). A promising agent for brain malignancies (it is able to cross the blood-barrier)

Measurements of dose-clonogenic survival curves of various tumor cell lines irradiated :

- at CNAO with a) protons and b) Carbon-ions
- at Istituto Tumori with photons,

combined or not with Epothilone B

Tumor Cell lines :

- **A549** (Non-Small Cell Lung Cancer)

(very frequent tumor in adults, leading cause of cancer related death in Europe)

- **U251MG** (glioblastoma)

(the most aggressive primary malignant brain tumor in adults)

- **Daoy** (medulloblastoma)

(the most common malignant brain tumor of childhood)

Equisurvival (~ 40%) Epothilone B concentrations used:

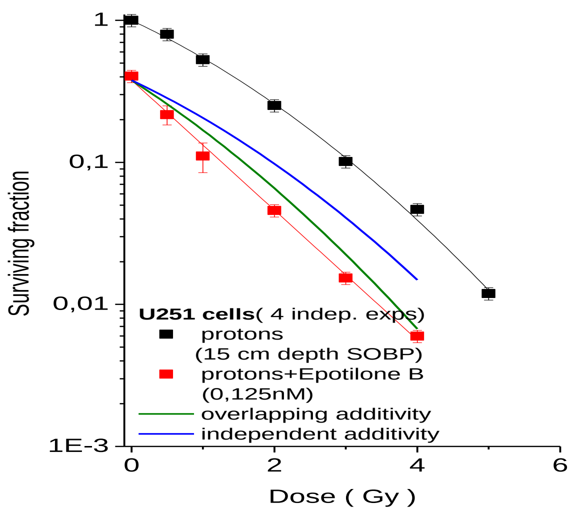
0.125 nM U251 MG
0.075 nM A549
0,035 nM Daoy

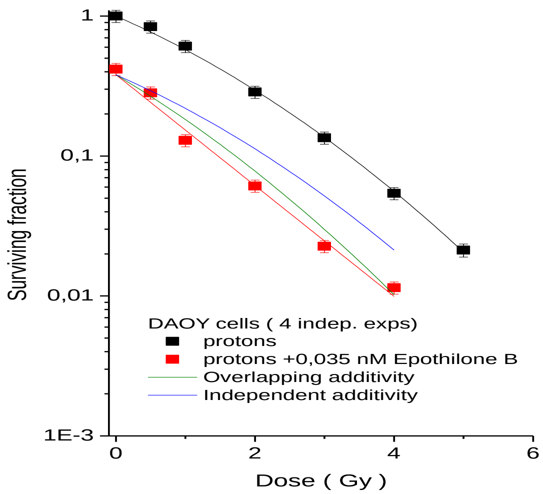
Invasive capacity , transwell invasion assay (QCM ECMatrixassay kit-24-well- Merk Millipore,8um)

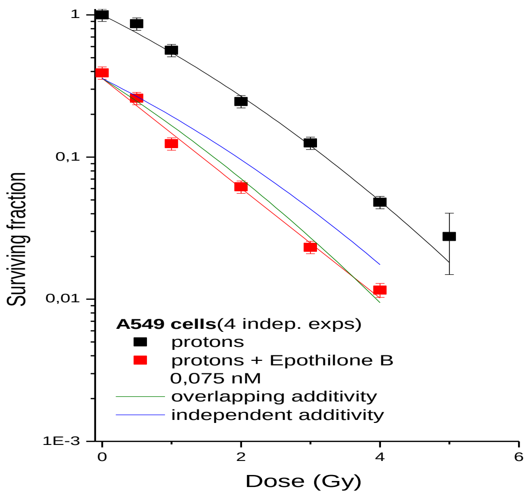
Epothilone B treated cells (compared to untreated ones) :
A549 55%
U 251 MG 68%

→ Epothilone B reduces A549 and U251cell invasive capacity

Survival of U251 MG , A549 and Daoy cells after Protons +/- Epothilone B treatment





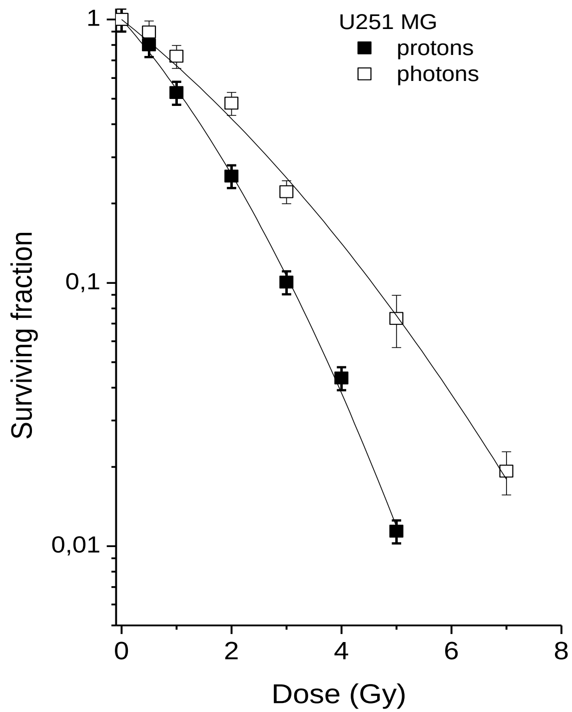


- **For all the cell lines Epothilone B increased protons (and photons, data not shown) cytotoxicity and the effect was more than additive.**

blue and green curves show calculated survival values for two additive interaction modalities: independent and overlapping (addition of Epothilone B equivalent to an additional radiation Dose D.*

Results on A549 and U251MG submitted for publication.

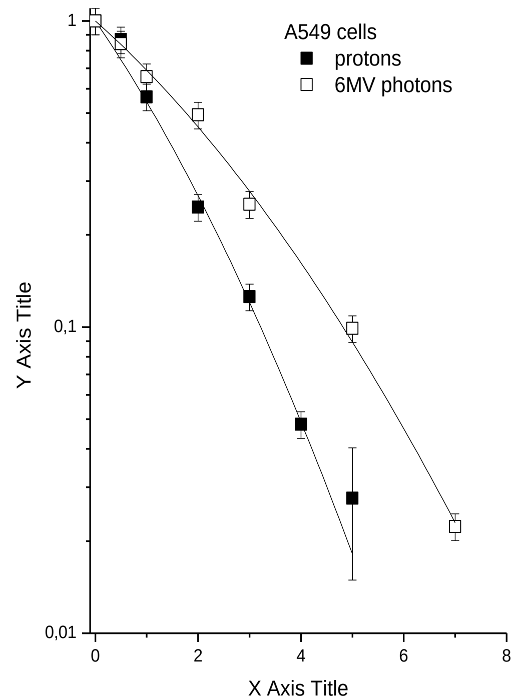
RBE of Protons (15 cm depth SOBP12_18 cm)



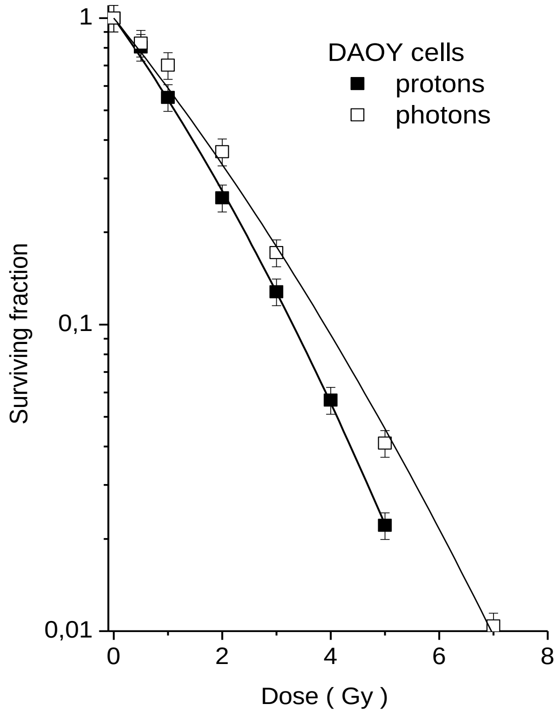
U251MG cells, protons and 6 MV photons

(4 independent exps)

RBE $_{10\%}$ = 1.4 +/- 0.2



A549 cells, protons and 6 MV photons
(4 independent exps)
RBE $_{10\%}$ = 1.5 +/- 0.2



DAOY cells, protons and 6 MV photons
(4 and 3 independent exps)
RBE $_{10\%}$ = 1.2 +/- 0.1

Proton RBE depends on the cell line and… it is Not always 1.1 !

In progress: Interaction of Epothilone B and C ions ; C ions RBE

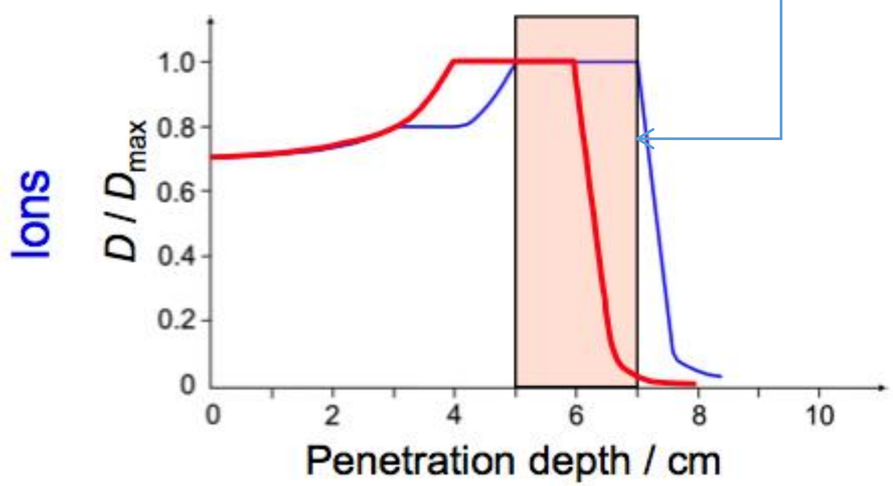
Range monitoring in Charged Particle Therapy

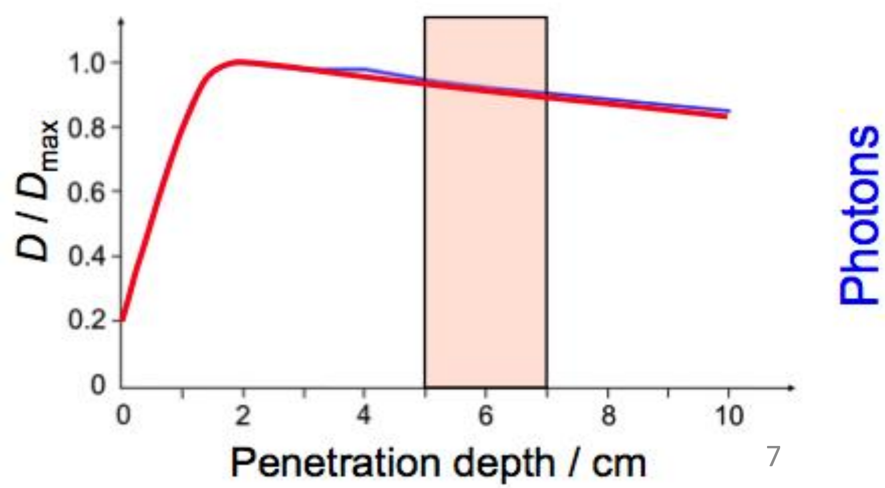
The peculiarity height dose release at the end of the range in CPT with respect to photon RT, make crucial the dose monitoring.

Inhomogeneities, metallic implants, CT artifact, HU conversion, inter session anatomical/physiological changes-> range variations

Effect of density changes in the target volume

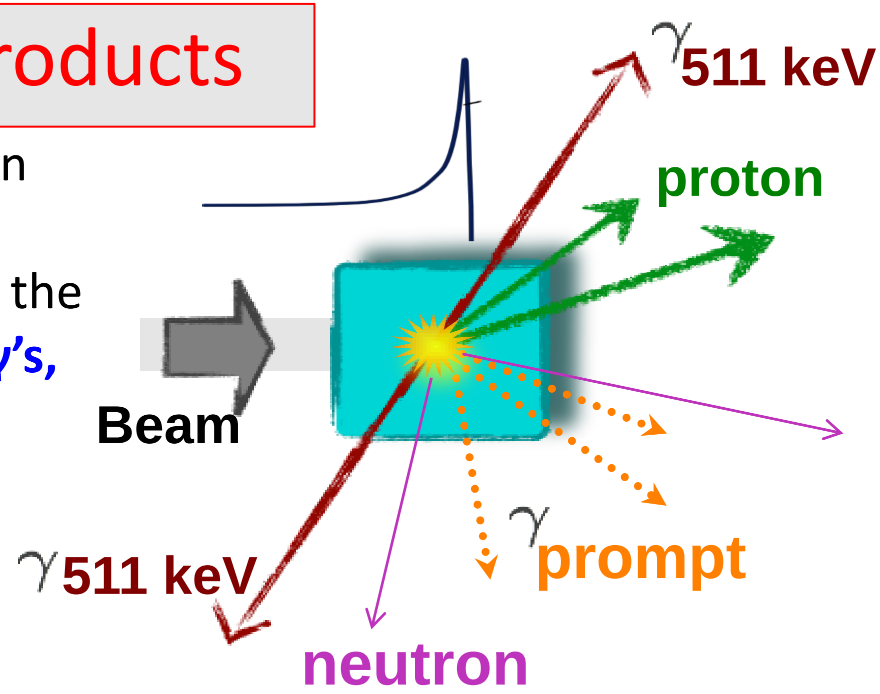
a little mismatch in range evaluation ➔ significant change for particle therapy with respect to X-ray radiotherapy





Beam range & secondary products

The p,^{12}C beam is dumped inside the patient. In order to monitor the beam the secondary particles generated by the beam interaction in the patient can be used: **prompt γ's, annihilation γ's, neutrons and charged particles**



Activity of β⁺ emitters

- Baseline approach
- Isotopes of short lifetime ^{11}C (20 min), ^{15}O (2 min), ^{10}C (20 s) with respect to diagnostic PET (hours)
- Low activity → long acquisition time (~minutes) with difficult in-beam feedback
- Metabolic wash-out of β^+ emitters

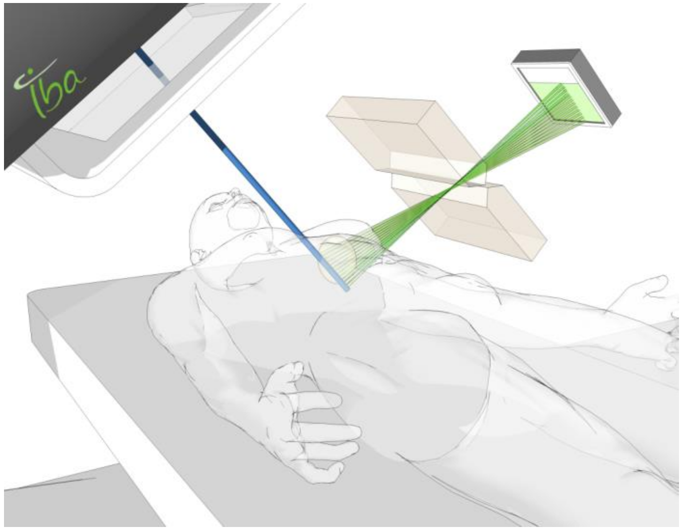
Prompt nuclear de-excitation γ's

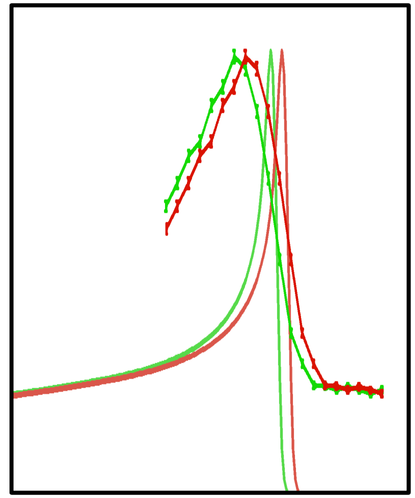
- ~1-10 MeV
- emission profile correlated with dose profile
- Specific detector at present under development: collimated slit cameras or Compton cameras

Charged secondary particles (ion therapy):

- The detection efficiency is almost one
- Can be easily back-tracked to the emission point -> can be correlated to the beam profile & BP
- They are forward peaked
- Enough energy to escape from patient
- MS inside the patient -> worsen the back-pointing resolution

A Prompt Gamma Camera for Real-time Range Control in Proton Therapy





Intended application:

Measurement of the position at which the proton beam stops in the patient in PBS mode

Camera configuration

Knife-edge slit collimation and 1D detection of γ-ray profiles

Points of attention:

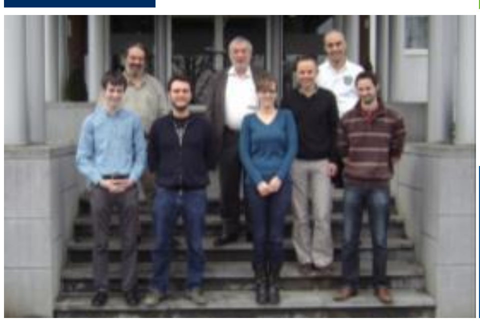
Simplicity, cost effectiveness

Collimator, software and project PI

UCL Université catholique de Louvain

imagX UCL & IBA

iba



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ULB

Detector and Electronics

POLITECNICO MILANO

XGLAB X and Gamma Ray Electronics

Clinical partner

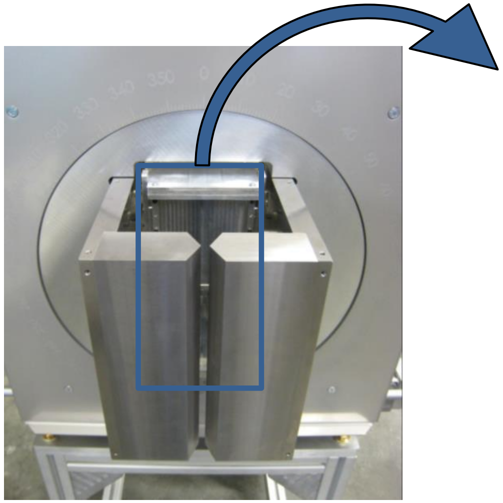
OncoRay National Center for Radiation Research in Oncology Dresden

TECHNISCHE UNIVERSITÄT DRESDEN

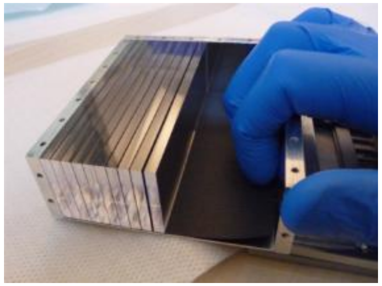
HZDR

and others…

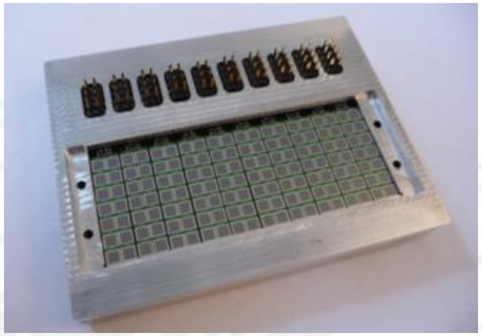
The Gamma camera: detector and electronics



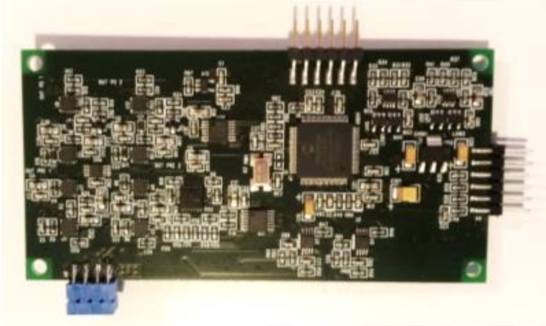
53 kg W collimator in 5:4 magnification for a 10 cm FOV



500 cm³ LYSO distributed in 2 rows of 20 slabs



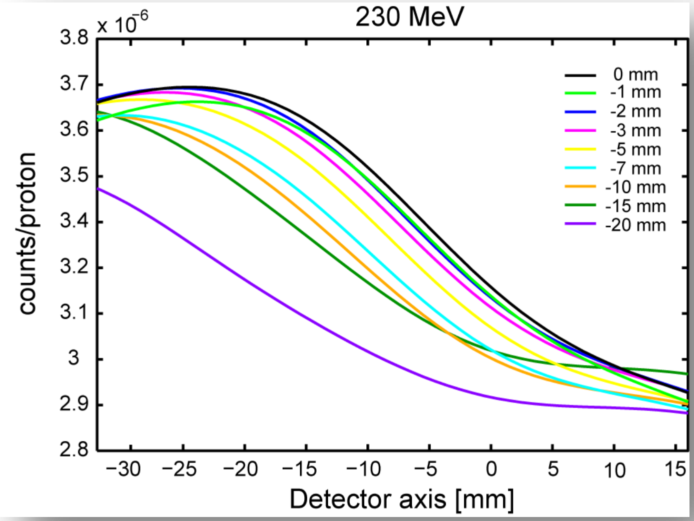
Light readout of one extremity of each LYSO slab by a row of 7 SiPM



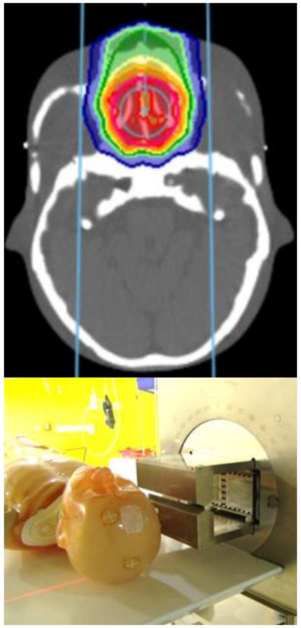
40 independent acquisition channels operating in two modes (slow calibration and fast counting)

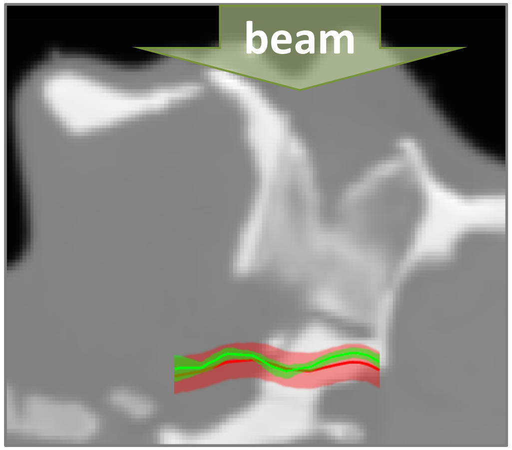
Experimental validation

Shift measurements



Nasal cavity





Planning uncertainty **> 5 mm**
(margin of 3.5% + 2 mm)
Measurement uncertainty (1.5σ)
≈ 2.0 mm

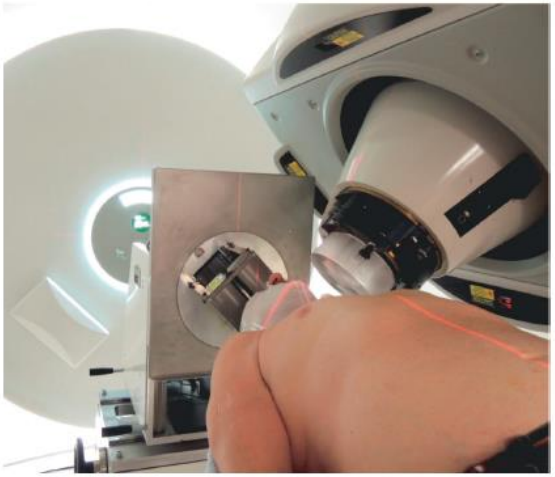


Fig. 1. PGI slit camera trolley (upper row) and its application during patient treatment (lower row).

Contents lists available at ScienceDirect

Radiotherapy and Oncology

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ELSEVIER

Original article

First clinical application of a prompt gamma based *in vivo* proton range verification system

Christian Richter [a,b,c,d,e,*], Guntram Pausch [a,b,c], Steffen Barczyk [a,b], Marlen Priegnitz [c], Isabell Keitz [a], Julia Thiele [b], Julien Smeets [f], Francois Vander Stappen [f], Luca Bombelli [g], Carlo Fiorini [h], Lucian Hotoiu [f], Irene Perali [h], Damien Prieels [f], Wolfgang Enghardt [a,b,c,d,e], Michael Baumann [a,b,c,d,e]

[a] OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Helmholtz-Zentrum Dresden – Rossendorf; [b] Department of Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden; [c] Helmholtz-Zentrum Dresden – Rossendorf; [d] German Cancer Research Center (DKFZ), Heidelberg; [e] German Cancer Consortium (DKTK), Dresden, Germany; [f] Ion Beam Applications SA, Louvain-la-Neuve, Belgium; [g] XGLab S.R.L., Milano; and [h] Politecnico di Milano, Dipartimento di Elettronica, Informazione e Bioingegneria, Italy

The

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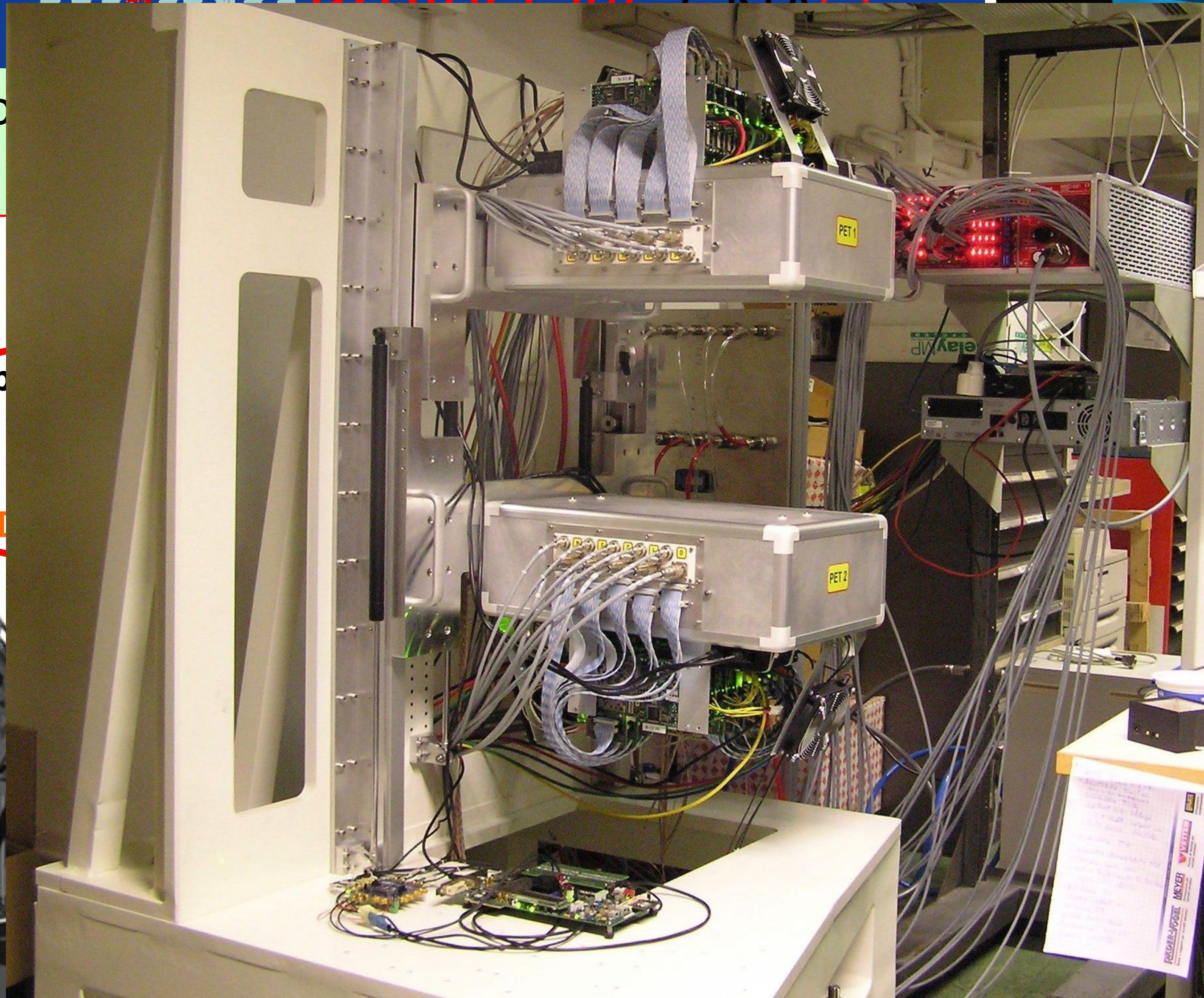

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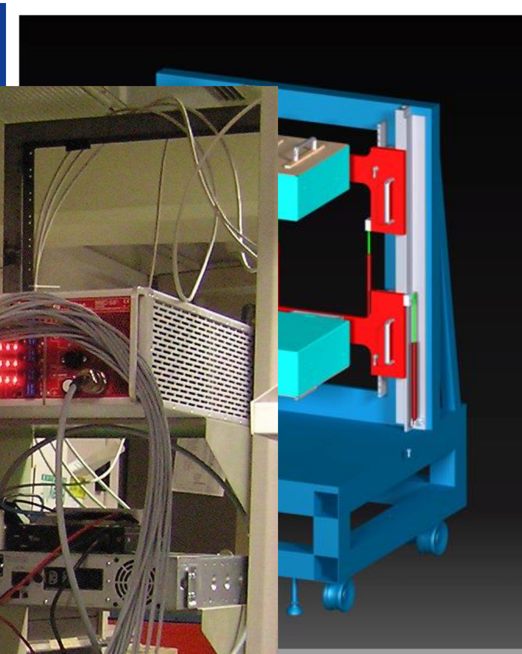
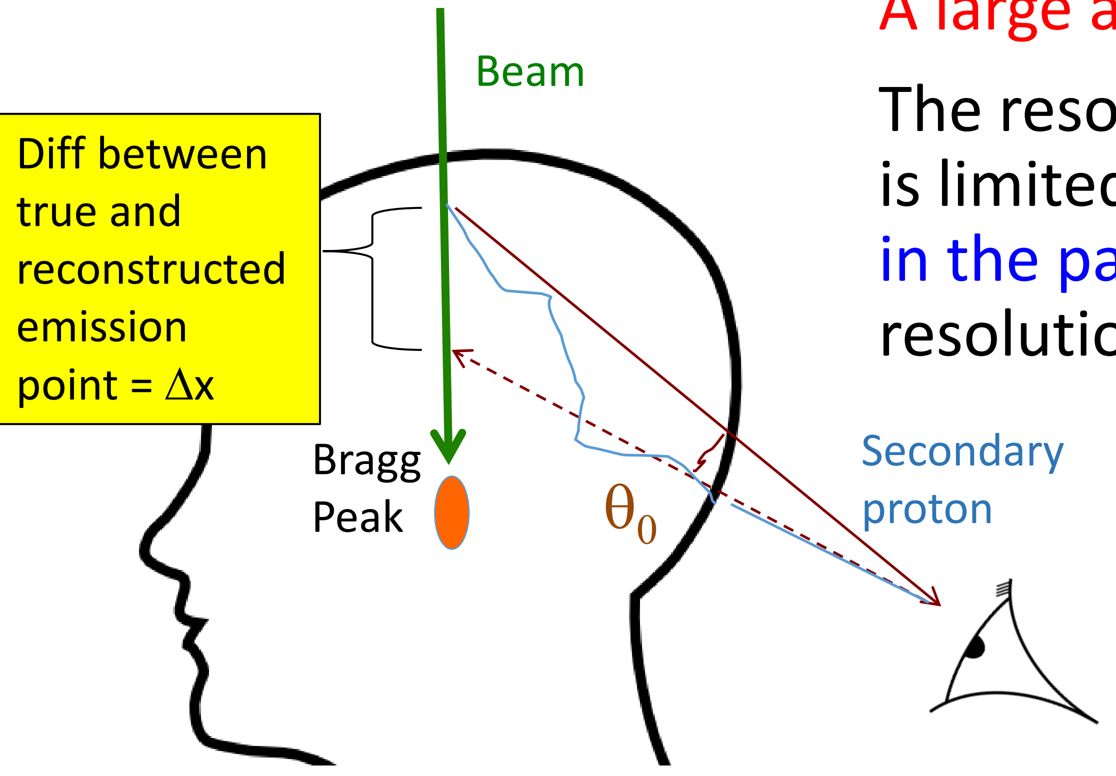


on the

- ✓ Effective both on proton and ^{12}C beam

Which detector should be used?



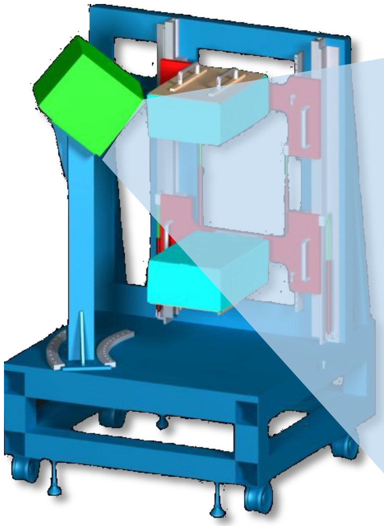
A large area detector.

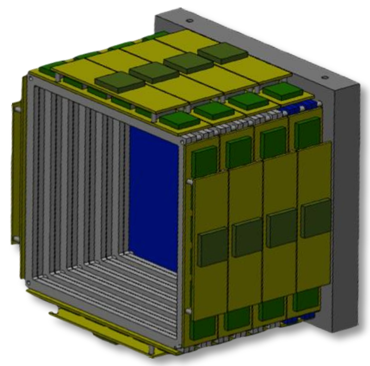
The resolution of the back-tracking is limited by the multiple scattering in the patient, not by the detector resolution.

Typical resolution on Dx is of the order of 6-8 mm

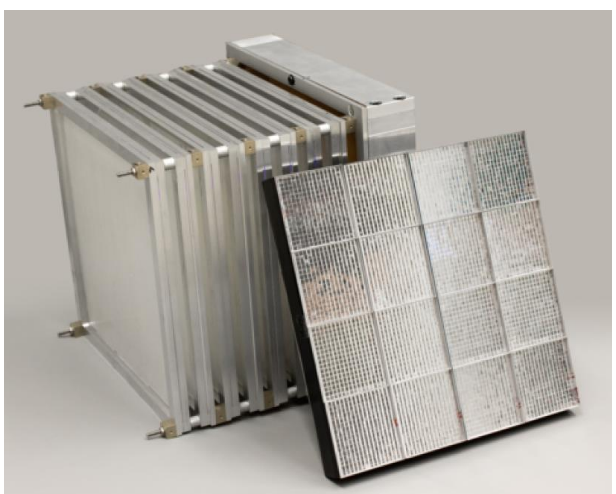
Integrating enough statistic (~ 10^3 events) helps to lower the accuracy on the emission point distribution (and then on the beam profile) to mm level ➔detector size

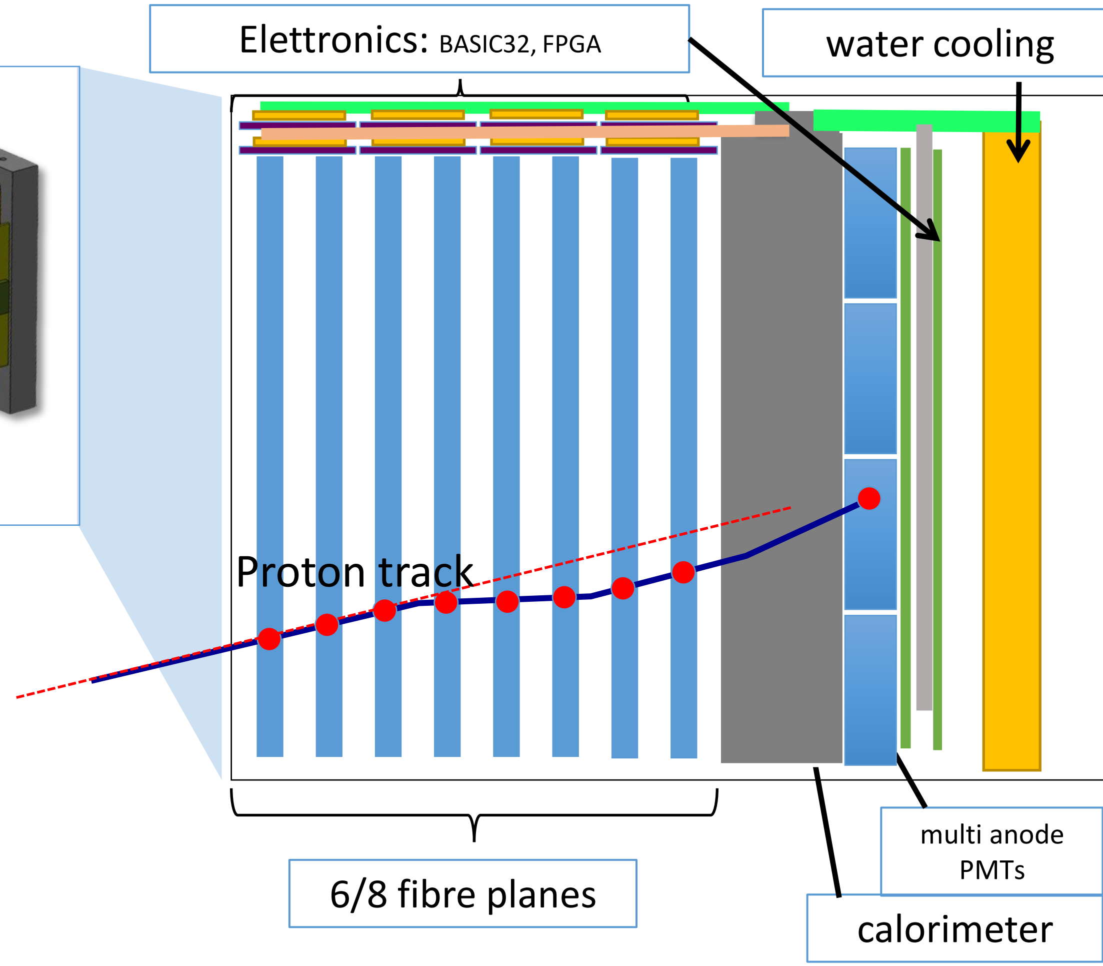
Dose Profiler (DP)





28 x 28 x 35 cm^3





- 6/8 planes of orthogonal squared **scintillating fibers** coupled to SiPMs
- a **calorimeter** coupled to Position Sensitive PMTs.

Development of Monte Carlo models and applications for medicine and hadrontherapy: the FLUKA code

G. Battistoni, P.R. Sala (INFN Milano)
in collaborazione con:
A. Ferrari et al. (CERN), A. Mairani et al. (CNAO), K. Parodi et al. (LMU/HIT), T. Boehlen (MedAustron).

Monte Carlo simulation codes are widely used because allow detailed description of radiation transport and interaction with matter, including nuclear interactions.

Among many other things, Monte Carlo codes allow:

- TPS verification and recalculation:
  - LET/dosimetry optimization/predictions for all ions
  - import CT images: -> detailed geometry and material description
  - accurate 3D description of dose distribution
  - predict secondary particle production
- Design of new facilities:
  - Possible beam line loss related calculations
  - Shielding calculation

The FLUKA MC code

http://www.fluka.org

Main authors: A. Fassò, A. Ferrari, J. Ranft, P.R. Sala

Contributing authors: G. Battistoni, F. Cerutti, M. Chin, T. Empl, M.V. Garzelli, M. Lantz, A. Mairani, V. Patera, S. Roesler, G. Smirnov, F. Sommerer, V. Vlachoudis

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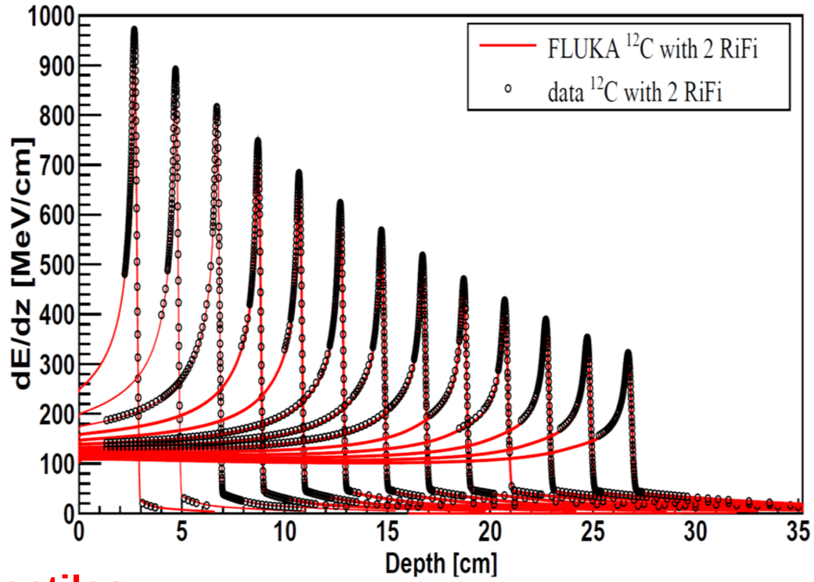
Main applications: Nuclear and Particle physics, Cosmic rays, Accelerator design (LHC systems), Particle detectors, Neutronics, Nucler waste transmutation, Dosimetry and Radiotprotection, Radiation damage, Shielding design

FLUKA for Hadrontherapy

HIT and CNAO (p and ^{12}C):

- **TPS data generation (Siemens, RaySearch…)**
- **TPS verification/optimization**
- **Plan robustness**
- **Research: new beam, therapy monitoring**
- **RBE comparison: NIRS vs. CNAO in carbon ion**
- **Eye treatments with active scanning**
- **Prompt γ's**
- **isotope production by protons and Carbon projectiles**

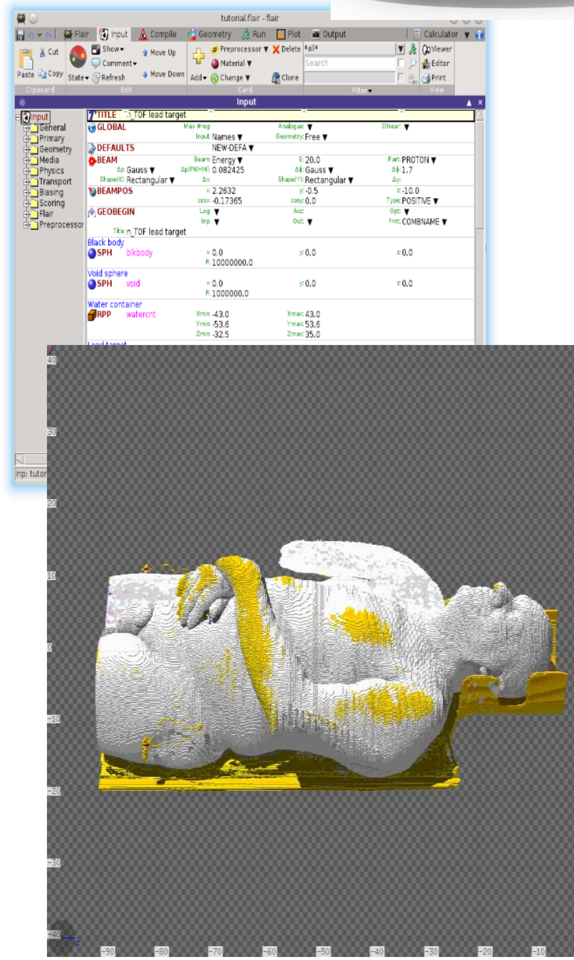
Clinical use! (TPS verification/optimization, Plan robustness)



Physics well established and already in clinical use, most emphasis now on tools

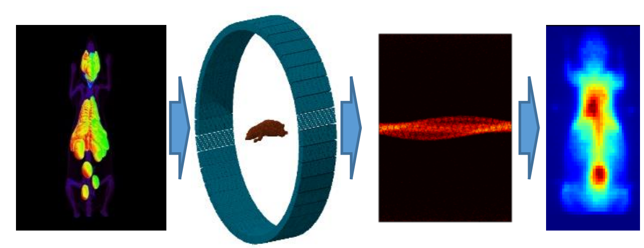
User interface (Flair)

- Medical oriented enhancements on the FLUKA interface:
  - DICOM CT, MR, importer
  - Automatic material assignment
  - Importing ROI RTstructures
  - Importing RTPlan
  - Generation of DVH plots and comparison plots with RTDOSE
  - Automatic PET scanner generator with predefined commercial templates, management of the scoring from FLUKA output and image reconstruction
- Running FLUKA simulations … with no programming skill or file editing requirement!

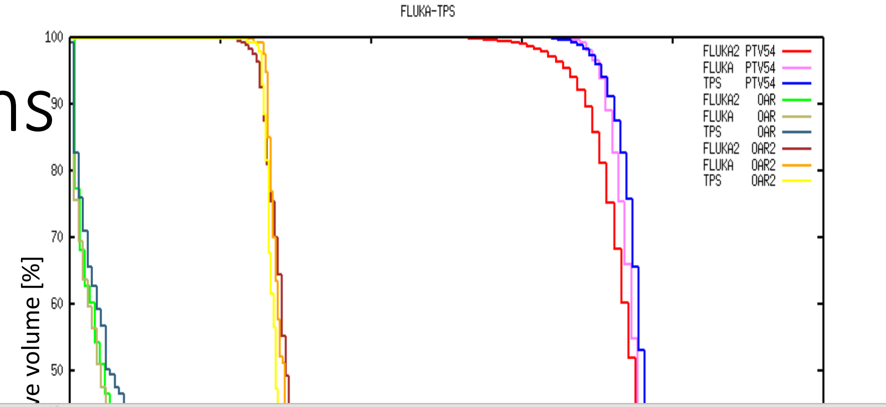


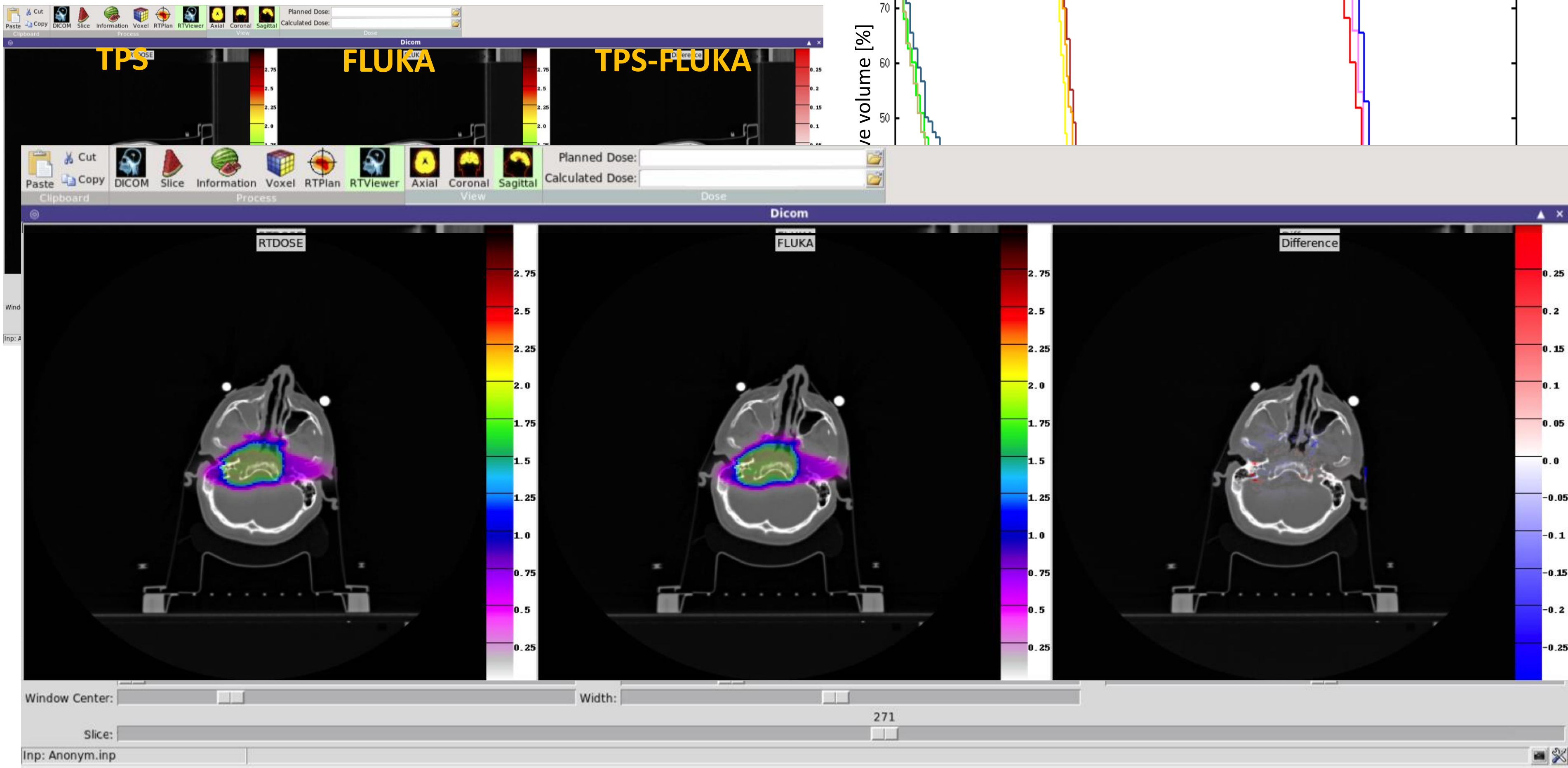
Short term goal: → Use FLUKA as Quality Assurance tool towards a (routine) clinical use

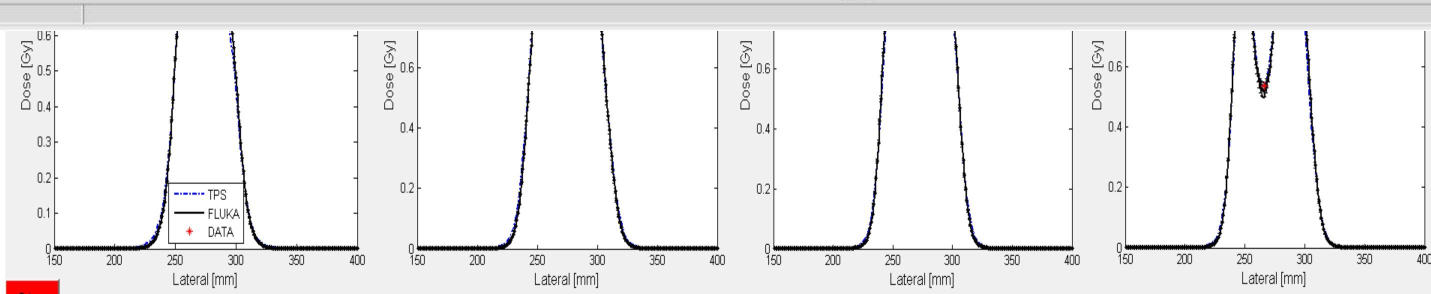
Long term goal: → Full MC (FLUKA) based TPS



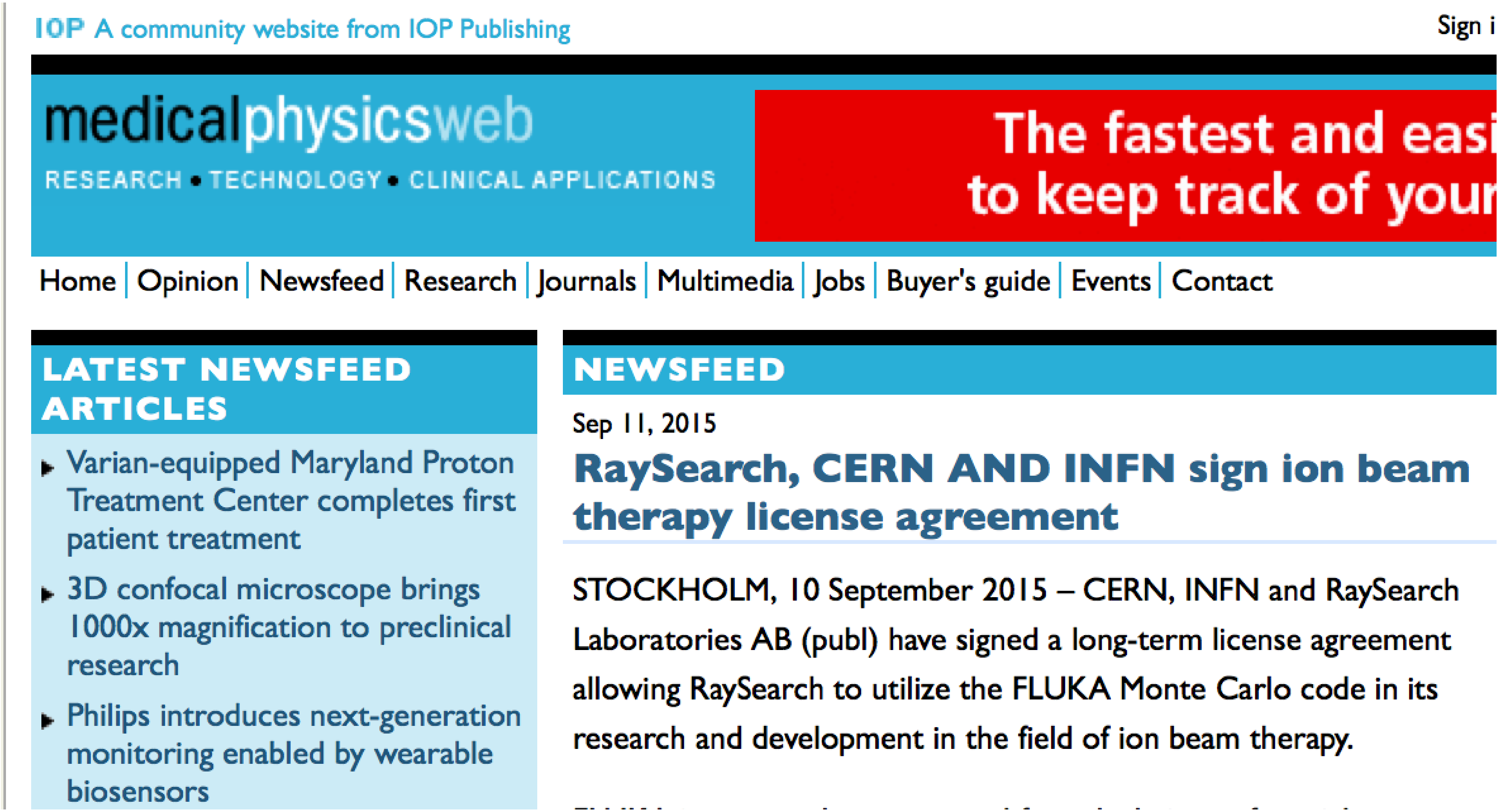
TP QA: example with protons







Industrial relationships



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- 3D confocal microscope brings 1000x magnification to preclinical research
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NEWSFEED

Sep 11, 2015

RaySearch, CERN AND INFN sign ion beam therapy license agreement

STOCKHOLM, 10 September 2015 – CERN, INFN and RaySearch Laboratories AB (publ) have signed a long-term license agreement allowing RaySearch to utilize the FLUKA Monte Carlo code in its research and development in the field of ion beam therapy.

Before Raysearch*: *Siemens, IBA, …

Ongoing activities

- Physics/dosimetry (and not only):
  - Continuous refining of physics models (in particular of nuclear interactions)
  - Very light ion beams (^{3}H, Li): develop/check the nuclear model physics
  - Different radiobiological parameters/models (e.g. health tissue/tumor)
  - Explore the possible use of ^{11}C/^{15}O beams
  - Monitoring: β^{+} production, prompt photons, charged particles
- Tool Development:
  - Facilitate the clinical use of FLUKA
  - Monte Carlo based treatment planning system (MCTPS)
  - Seamless integration and presentation of expected PET, prompt photons, charged particle signals
  - Quality assurance
  - Region-Of-Interest implementation
  - (Software) acceleration techniques
  - Exploiting new HW capabilities (Vector programming, Intel Phi, GPU's etc)?

Progetto L3IA (2016-2018)

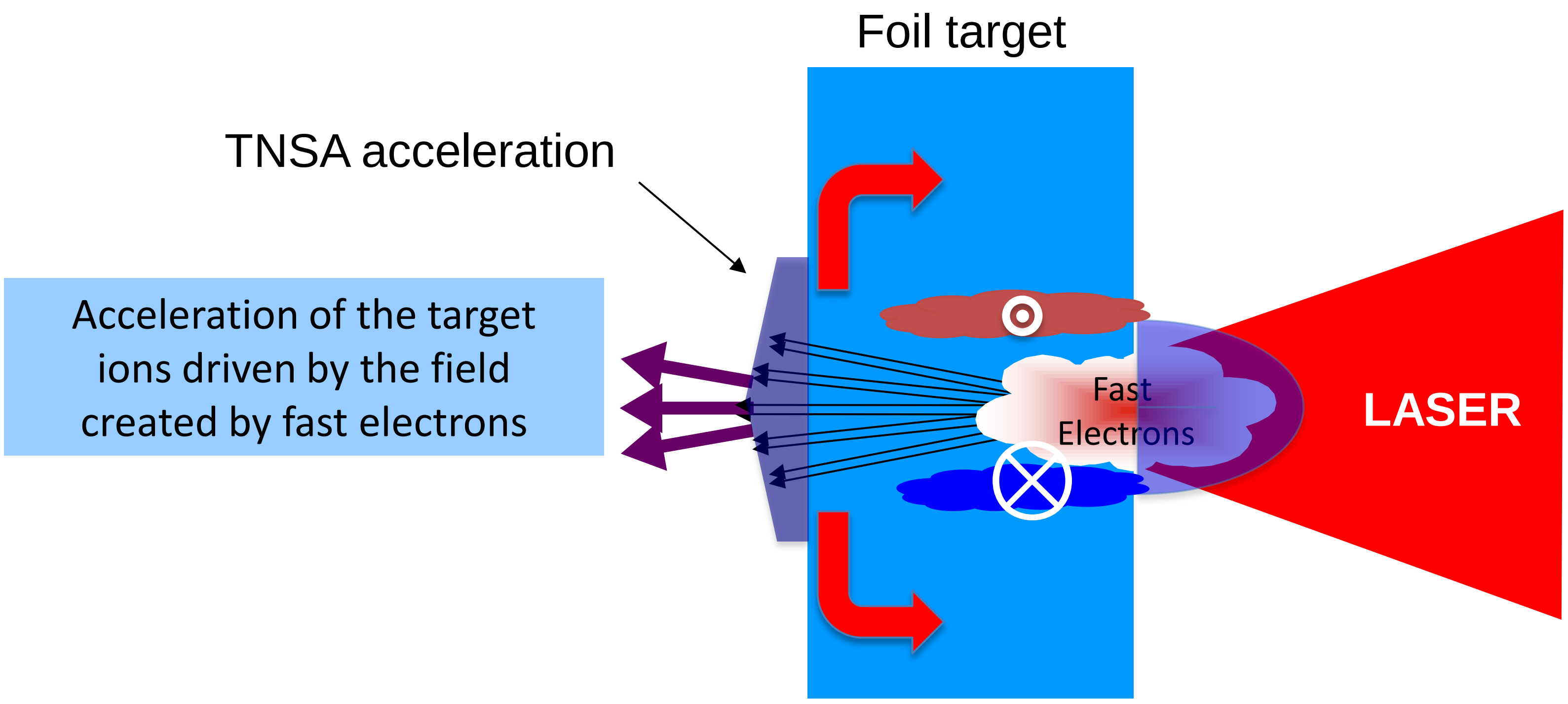
Line for Laser Light Ion Acceleration

Finanziato da CSN5 INFN con partecipazione Sezioni Milano, Pisa, LNS, Bologna, Napoli

P.I. Dario Giove – INFN Milano
Leo Gizzi – CNR & INFN Pisa

Target Normal Sheath Acceleration

Laser-foil interactions creates huge currents of relativistic eletrons propagating in the solid and giving rise to intense X-ray emittion and, ultimately, ion emission from the rear surface of the foil



R.A.Snavely et al., Phys. Rev. Lett. **85**, 2945 (2000)
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J. Fuchs et al. Nature Physics **2**, 48 (2006).
X.H.Yuan et al., New Journal of Physics **12** 063018 (2010)

INFN

Laser driven ion acceleration

- High gradient acceleration: MeVμm−1, compared with ∼MeV m−1 provided by radio frequency (RF) based accelerators;
- Ultra-short duration at the source of the ion bunch of the order of picoseconds;
- Very small effective source size: ≈10 μm;
- highly laminarity and very low emittance;
- Broad energy spectrum
- High charge: 10^{8}-10^{9} particles

Project Main Issues

- European test facility for laser based proton and light ion acceleration mechanisms (within 2018 12-15 MeV proton beams; at the end of 2016 expected stable 5 MeV beams with a maximum repetition rate @ 1 Hz)
- Accelerator studies for a new generation of sources without RF powered components
- Beam manipulation and diagnostic
- Dosimetry and radiobiology: fast (ps) ion source to be investigated for future hadrotherapy plants

Current effort

- New acceleration mechanisms at ultrahigh intensity
  - Radiation pressure acceleration
  - Collisionless shock acceleration
- Target engineering: surface, geometry, conductivity
- Post acceleration: selection, collimation, injection
- Dosimetry and radiobiology: fast (ps) ion source

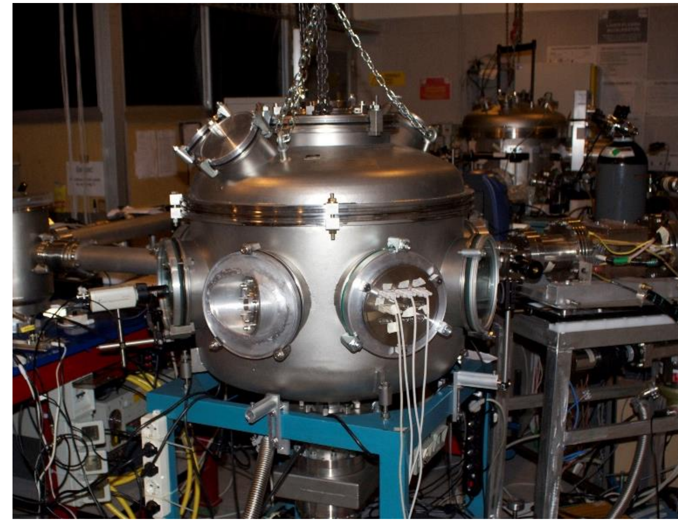
INFN

Current laboratory activity

Since October 2014 in Pisa new experimental chamber “Pavone” is operational for laser-solid interaction, dedicated to:

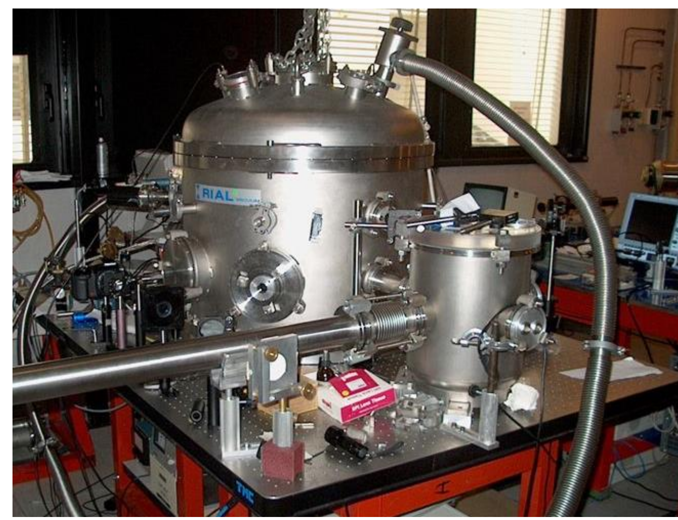
1. TNSA acceleration of light ions;
2. Fast electron transport;
3. Shock generation in nanoengineered target;
4. X-ray generation and applications

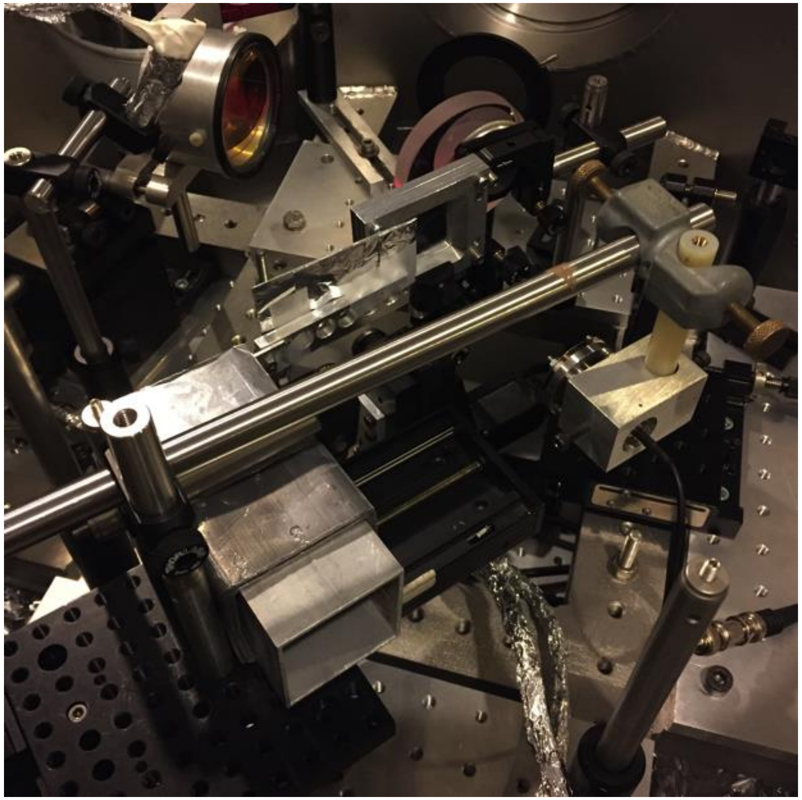
Proton beams of nearly 2.3 MeV obtained and measured with a 10 TW laser. The laser will be upgraded to 100 TW within the end of 2016

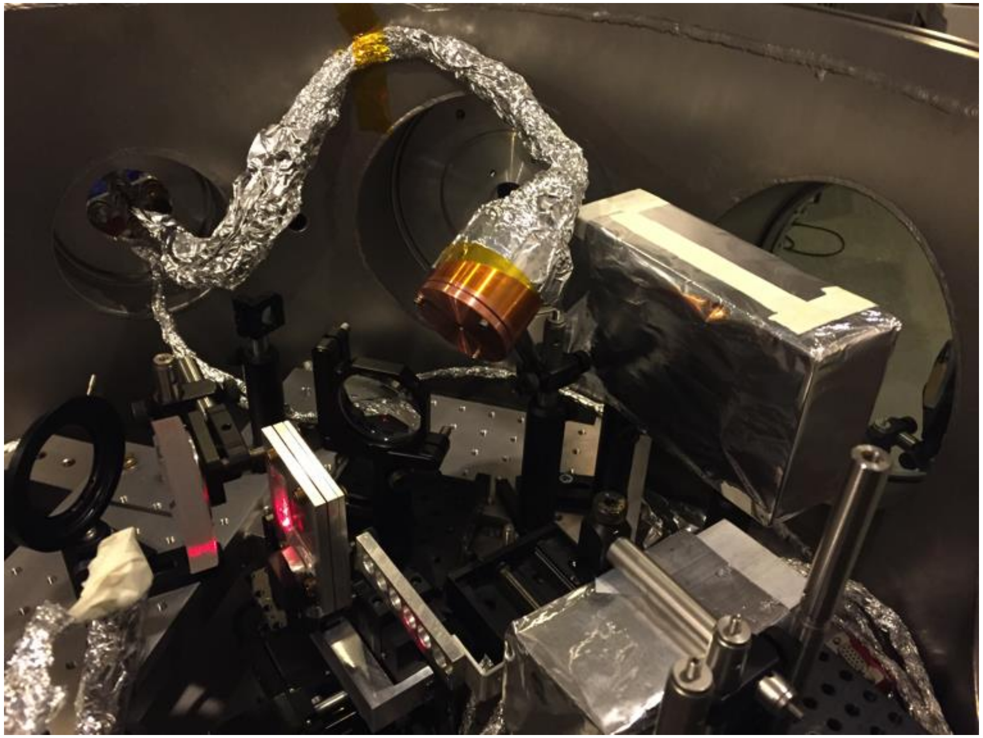


A separate target chamber is dedicated to laser-gas interaction for:

1. electron acceleration with self injection,
2. radiobiology applications
3. γ-ray generation (Thomson scattering and bremsstrahlung)







INFN

Detectors @ 45 mm from the target

A silicon microdosimeter for radiation quality assessment

S. AGOSTEO [1,2], C.A. CASSELL[2,3], A. FAZZI [1,2],) M.V. INTROINI [1,2], M. LORENZOLI [1,2],
A. POLA [1,2], E. SAGIA[2,3], V. VAROLI [1,2].

[1] INFN, Sezione di Milano, via Celoria 16, 20133 Milano, Italy.

[2] Politecnico di Milano, Dipartimento di Energia, Sezione di Ingegneria Nucleare CeSNEF, via Ponzio 34/3, 20133 Milano, Italy.

[3] ARDENT project.

MICRODOSIMETRIC SPECTRA: TISSUE-EQUIVALENCE AND GEOMETRICAL CORRECTIONS

In order to derive microdosimetric spectra similar to those acquired by a TEPC (Tissue Equivalent Proportional Chamber), corrections were studied and discussed in details [1,2]

Tissue equivalence of silicon

The telescope allows to optimize the tissue equivalence correction by measuring event-by-event the energy of the impinging particles and by discriminating them.

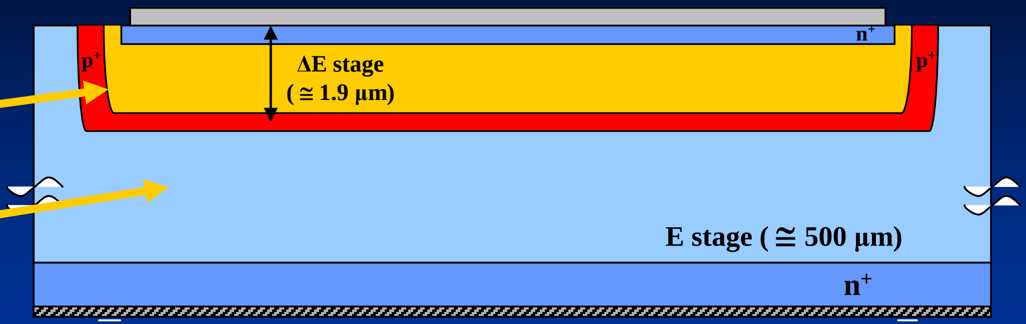
Shape equivalence

By following a parametric criteria given in literature, the lineal energy y was calculated by considering an equivalent mean cord length.

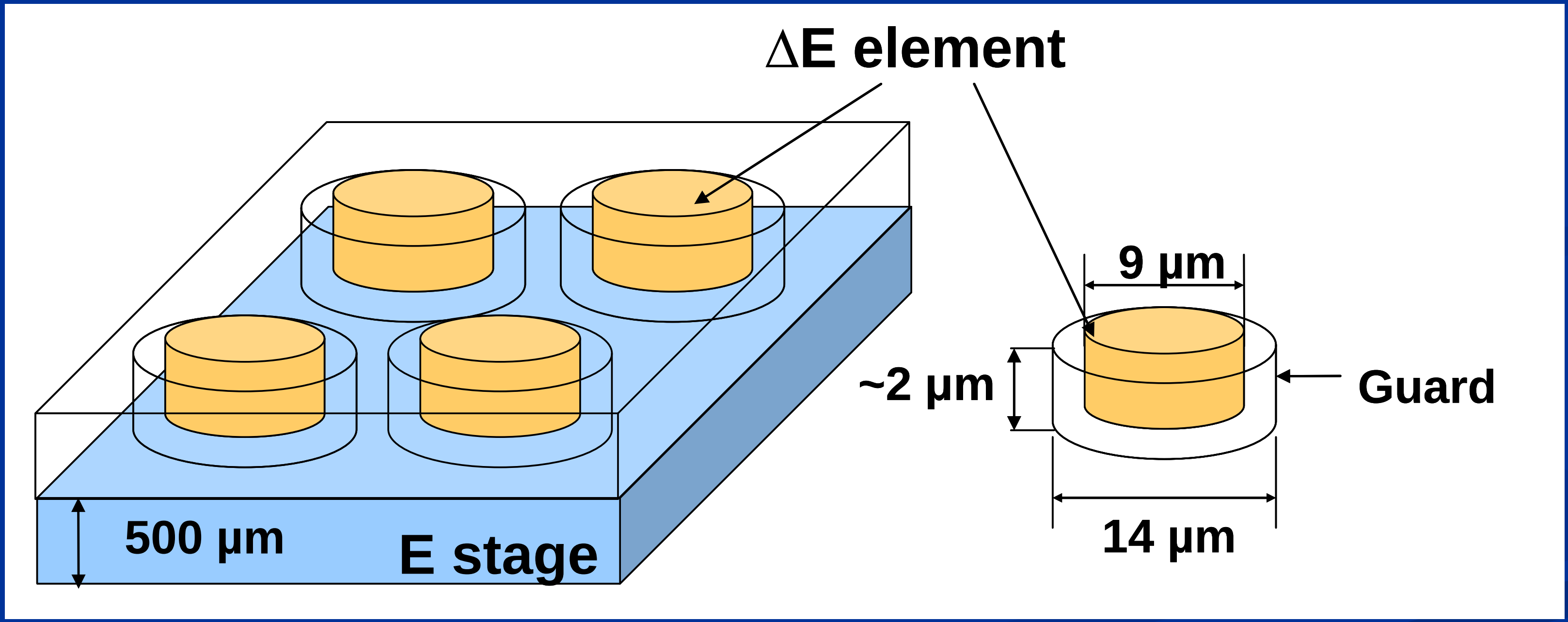
1. S. Agosteo, P. Colautti, A. Fazzi, D. Moro and A. Pola, "**A Solid State Microdosimeter based on a Monolithic Silicon Telescope**", Radiat. Prot. Dosim. 122, 382-386 (2006).
2. S. Agosteo, P.G. Fallica, A. Fazzi, M.V. Introini, A. Pola, G. Valvo, "**A Pixelated Silicon Telescope for Solid State Microdosimeter**", Radiat. Meas. 43, 2-6, 585-589 (2008).

SEGMENTED SILICON TELESCOPE

Silicon telescope:
a thin **ΔE stage** (1.9 μm thick)
coupled to a residual energy
stage E (500 μm thick)
on the same silicon wafer.



ΔE stage: matrix of cylindrical diodes (h= 2 μm , d= 9 μm)



More than 7000 pixels are connected in parallel to give an effective detection area of the ΔE stage of about 0.5 mm^2

RESPONSE TO PROTONS:

Irradiations with62 MeV modulated proton beam at CATANA facility (LNS-INFN Catania) and comparison with cylindrical TEPC (De Nardo et al., RPD 110, 1-4 (2004))

Results:

- easy-of-use system;
- rapid data processing;
- good measurement repeatability;
- high spatial resolution;
- good agreement at lineal energies higher than 7-10 keV μm^{-1}up

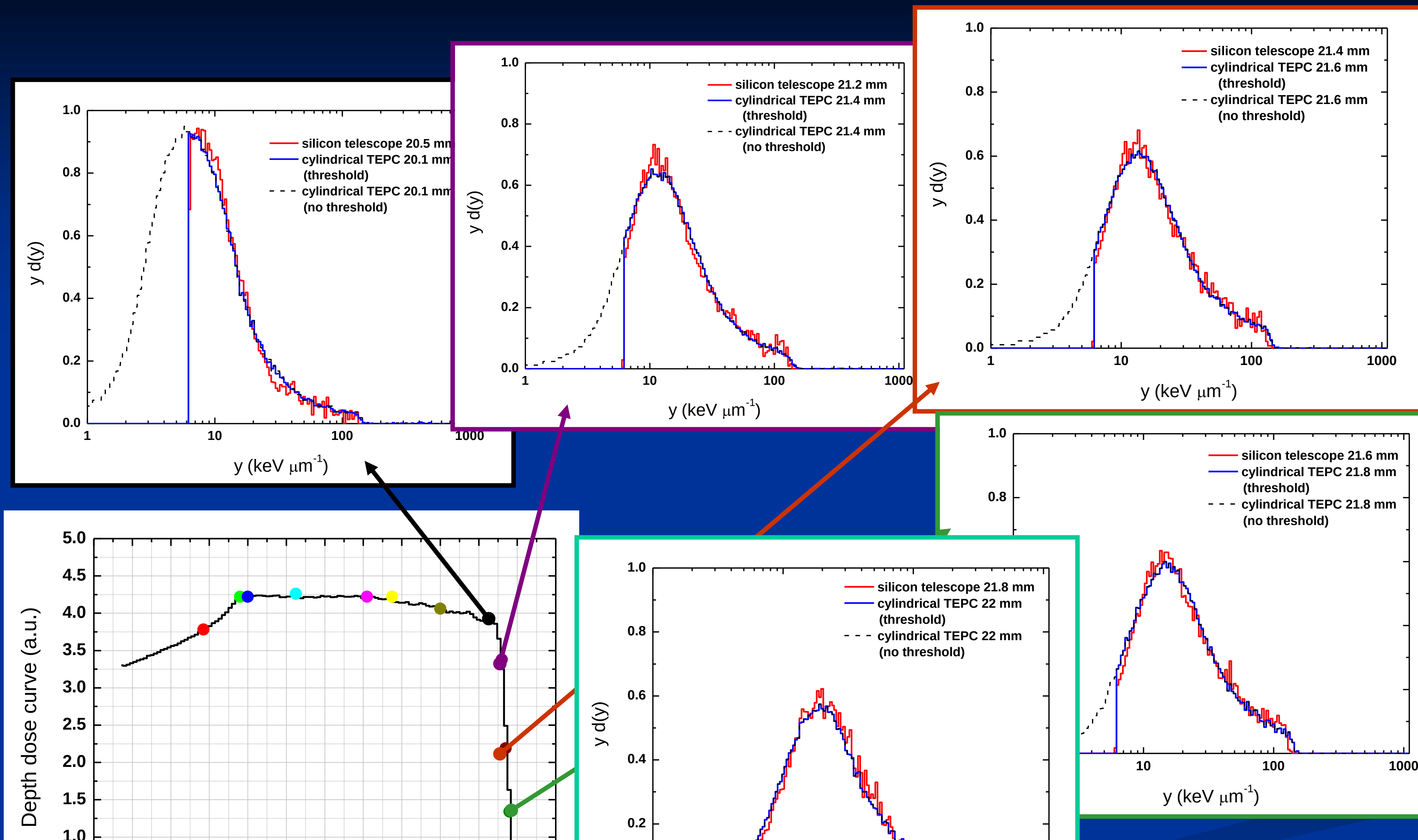
Limitation to be improved:

- electronic noise and count rate capability

Issues:

- accurate estimate of dose profile;
- radiation damage.

Comparison with cylindrical TEPC: distal part of the SOBP



Event-by-event TE correction, shape equival.

RESPONSE TO CARBON IONS:

Irradiations with
62 MeV/u un-modulated carbon beam at CATANA facility
(LNS-INFN Catania)

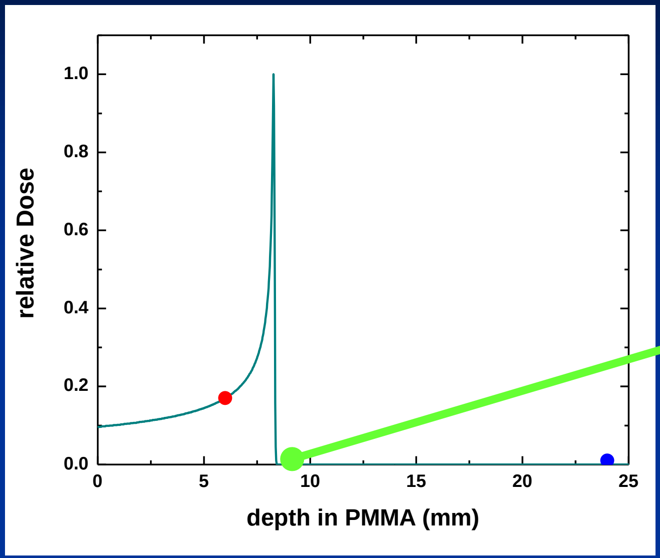
Results:

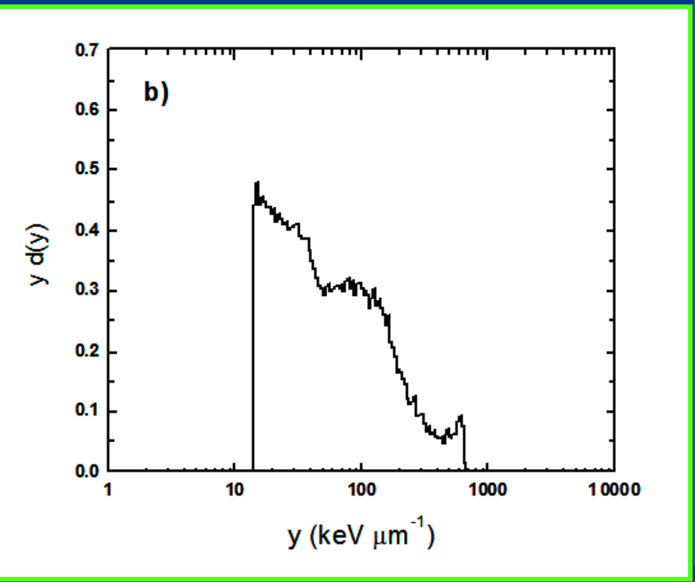
- high spatial resolution;
- capability of operating in a complex and intense radiation field;
- discrimination capability and potentialities.

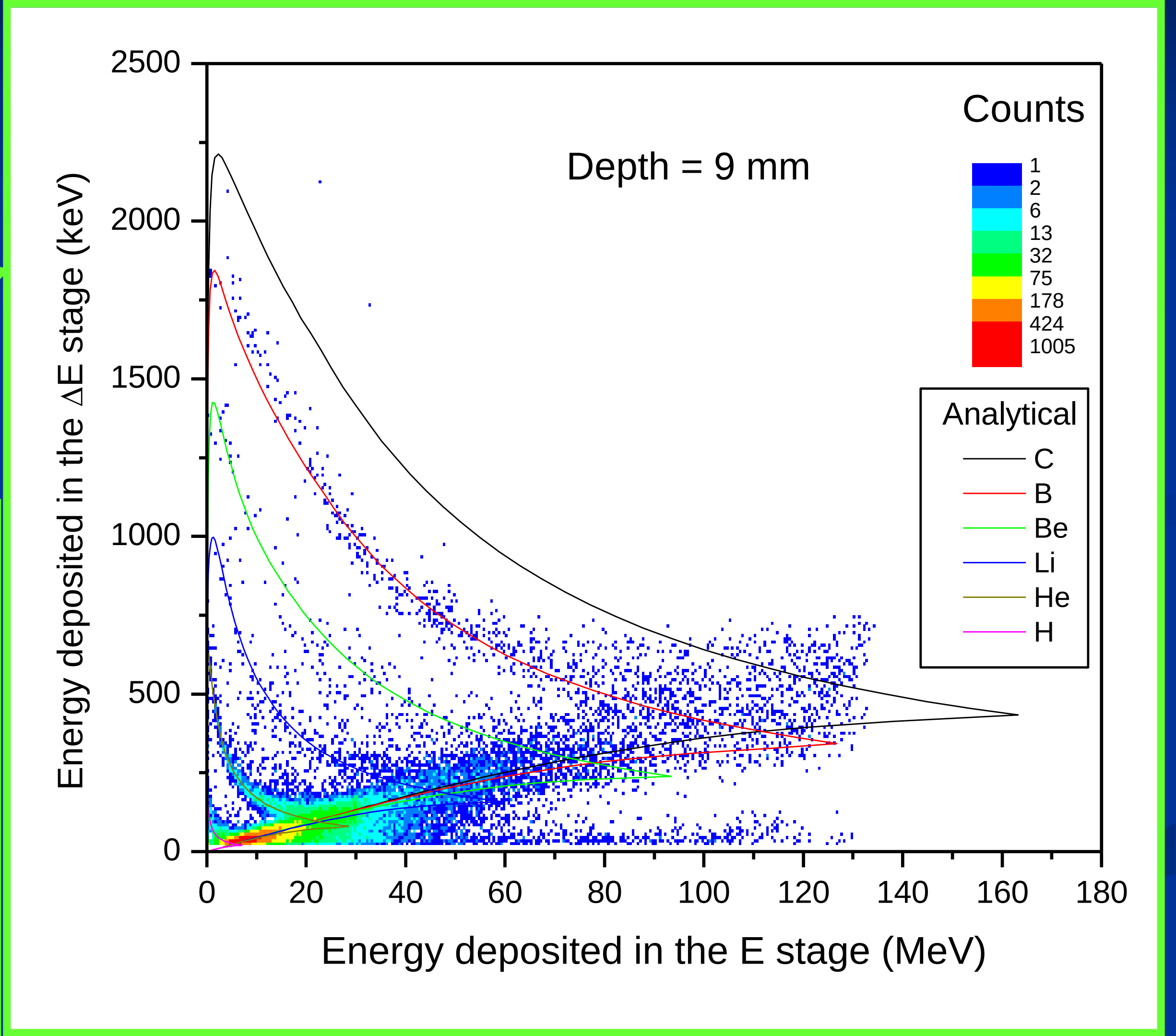
Problems to solve or to minimize:

- counting rates and radiation damage.

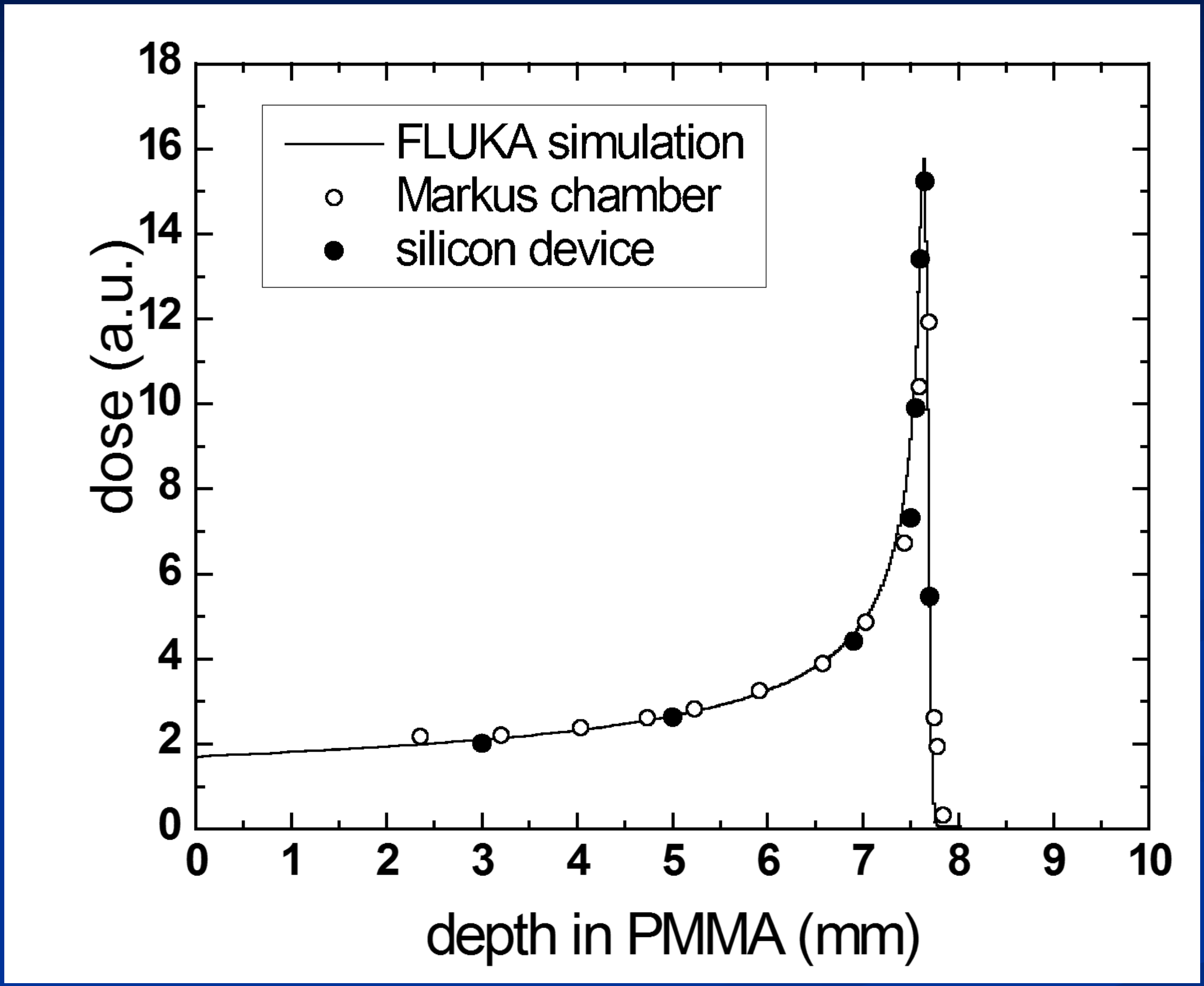
62 MeV/u un-modulated carbon beam (CATANA)



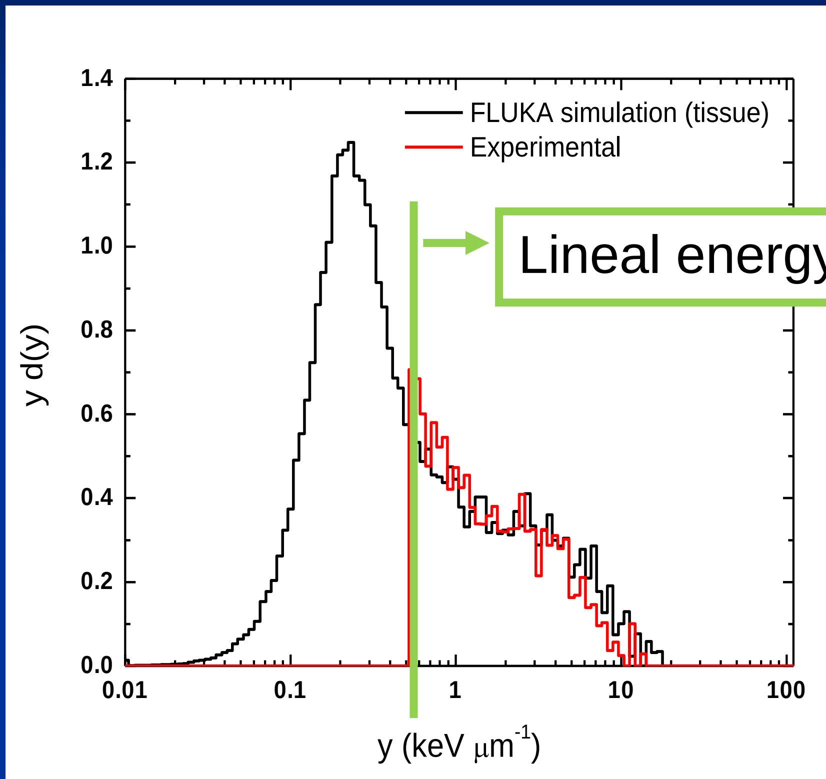




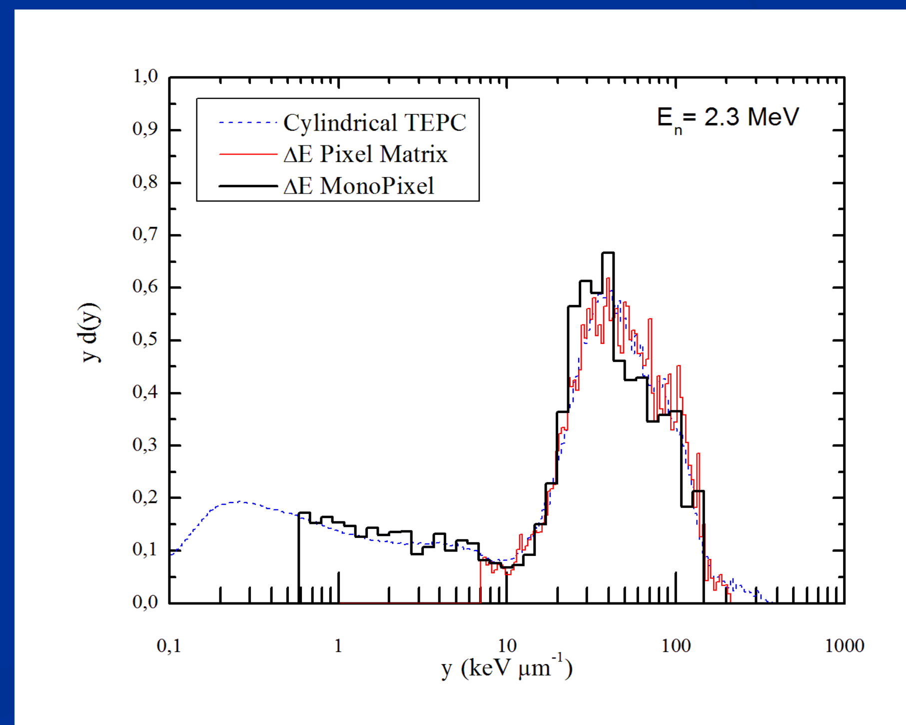
62 MeV/u un-modulated carbon beam (CATANA)



Improvement of the energy threshold: Test of the tissue-equivalence correction procedure for electrons And Irradiation with 2.3 MeV neutrons at LNL CN facility



Lineal energy threshold ≈ 0.6 keV μm^{-1}



NON CONVENTIONAL PRODUCTION OF RADIONUCLIDES BY PARTICLES ACCELERATORS FOR BIOMEDICAL APPLICATIONS

F. Groppi, M.L. Bonardi, S. Manenti, E. Sabbioni

Radiochemistry Laboratory, LASA,

Universita' degli Studi di Milano and

INFN Sez. Milano and Legnaro

e-mail: flavia.groppi@mi.infn.it

Relevant applications of radiotracers and labelled compounds in No Carrier Added form

some relevant applications

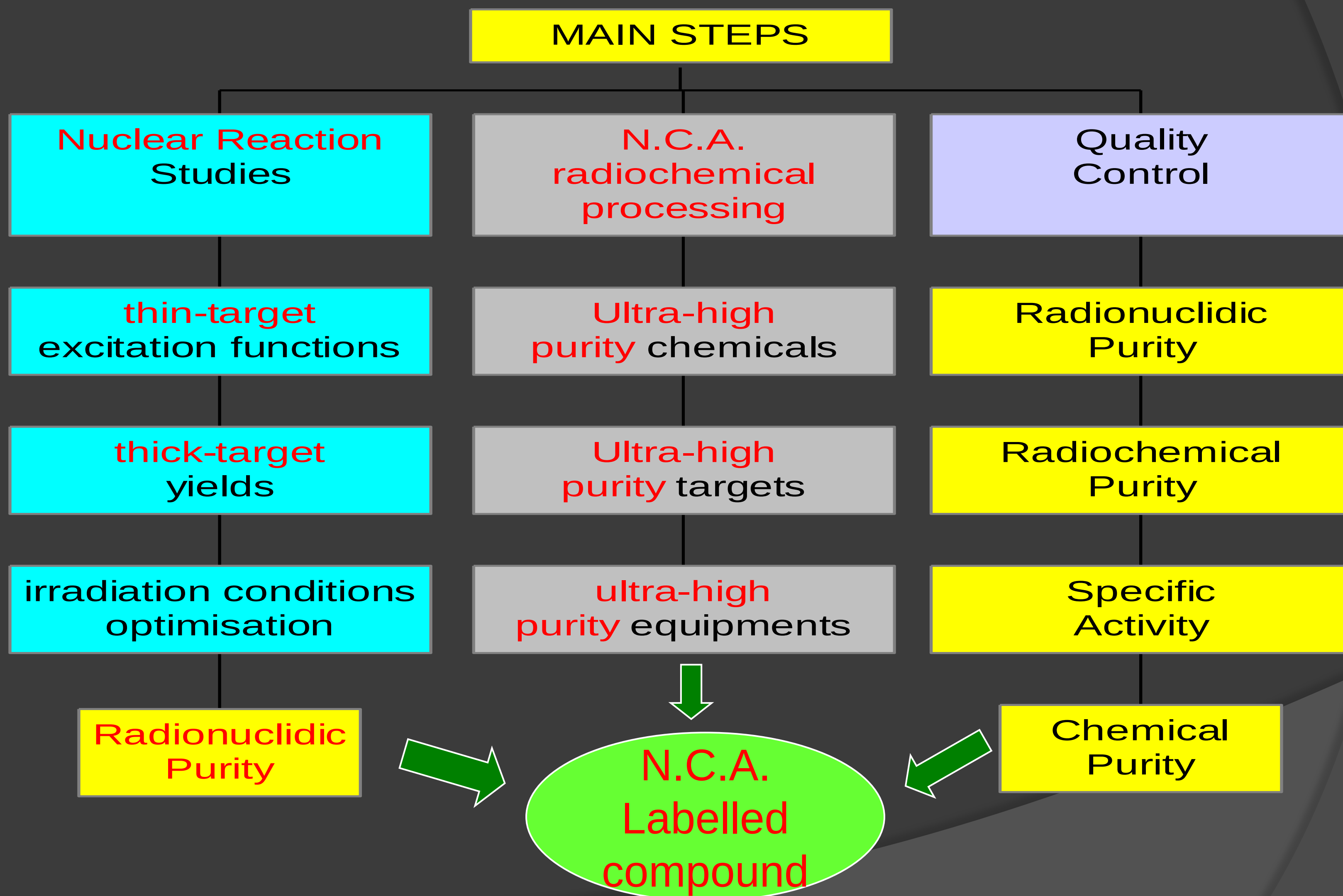
1. metallo-biochemistry **2. cellular biology**	**environmental toxicology at low doses**	**1. nuclear medicine** **2. metabolic radiotherapy**
behaviour of **different chemical forms** of **trace elements**	**Low Level** and **Long Term Exposure** (LLE) to **ultra-trace elements**	radiodiagnostics (SPECT, PET) systemic radionuclide tumour radiotherapy
speciation studies **synergistic effects**	**speciation studies** **dose-effect relationships**	radioimmunotherapy of tumours

F.Groppi, M. Bonardi, S. Manenti, E. Sabbioni - UNIMI & INFN MI

THERAGNOSTIC MEDICINE

- Theranostic medicine is a new integrated therapheutic system which can diagnose, deliver targeted therapy and monitor the response to therapy.
- the nuclear physician can follow the real biodistribution of the radiopharmaceutical inside the patient after the injection and the follow-up during the repeated treatments.
- The radioisotopes used for metabolic radiotherapy are α, β and Auger electron emitters. Many of them are also γ emitters and can be detected by gamma-camera, SPECT or PET.
- Many of these "neutron reach" radionuclides are produced by nuclear reactor with a very low specific activity - A_S. In selected cases they can be produced by bombardment of targets by charged particle beams, in No Carrier Added Form – NCA - with very high A_S

Production, Radiochemical Processing and QC/QA of *No Carrier Added* (n.c.a.) labelled species



Moreover the experimental determination of:

- ✓ **Biological Purity (for applications in the life sciences, biological and human)**

- ✓ **Stability vs. Time of all previous parameters, both *in-vitro* and *in-vivo***

Specific Activity determination techniques

Any "**elemental analysis**" technique combined with any kind of "**radiometric technique**"

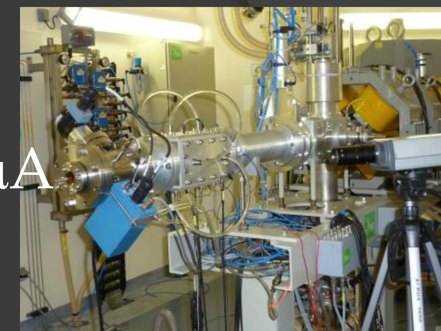
- **Atomic absorption** (GF-AAS), **atomic emission** spectrometries (ICP, ICP-MS)
- **Elettroanalytical** (ASV, CSV)
- **Mass spectrometric** (many kinds)
- **Neutron** and **charged particle activation analysis**, both instrumental and radiochemical
- **Radio-release** techniques
- **High-resolution X, γ, β, α spectrometries**
- **Liquid Scintillation Counting** (LSC)

Hyphenated techniques → ***Goal***

Involved laboratories

The research activity of the Milano Group is carried out at the following laboratories:

ARRONAX Cyclotron (Nantes)



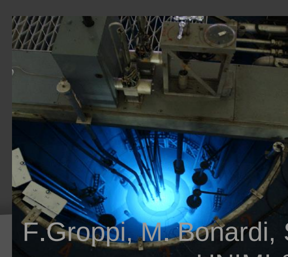
Beam particles

- Protons: 35 - 70 Mev up to 750 μA
- Deuterons: 15 – 35 Mev
- Alpha : 70 MeV

LASA → Radiochemistry Laboratory

LASA → Physics and Chemistry Measurements Laboratory

LENA - Pavia → Nuclear Reactor TRIGA MARK II



Radionuclides for metabolic radiotherapy and theragnostics

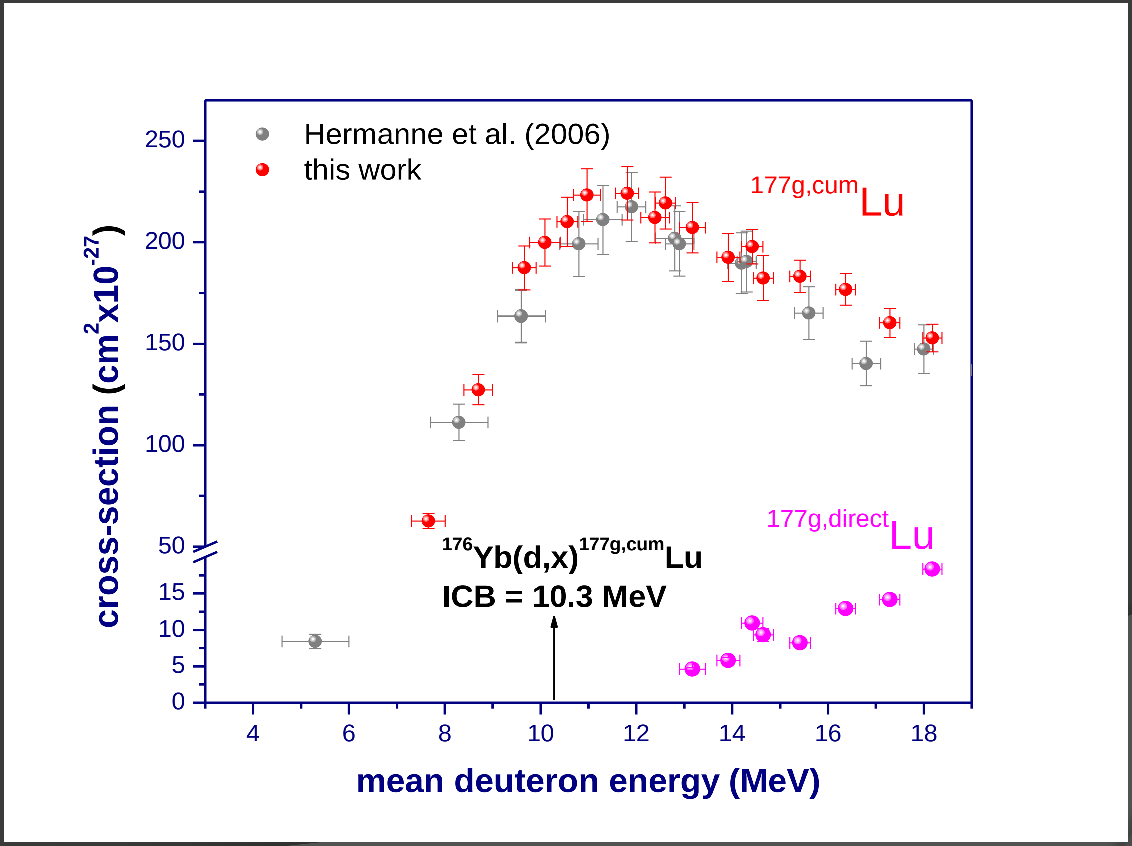
radionuclide	Half-life days	β-max MeV	R soft tissue mm	Eγ keV
Dy-165	0.1	1.29 (83%); 1.19 (15%)	5.7	95 (4%)
Sm-156	0.4	0.7 (51%); 0.4 (44%)		none
Re-188	**0.7**	**2.12 (72%); 1.96 (25%)**	**11.0**	**155 (15%)**
Ho-166	**1.2**	**1.85 (51%); 1.77 (48%)**	**8.5**	**81 (6%)**
Rh-105	1.5	0.57 (75%); 0.25 (20%)		319 (19%)
Sm-153	**1.9**	**0.67 (78%); 0.81 (21%)**	**2.5**	**103 (28%)**
Au-198	2.7	0.96 (99%)	3.6	411 (96%)
Y-90	**2.7**	**2.28 (100%)**	**11**	**none**
Re-186g	**3.7**	**1.07 (74%); 0.93 (21%)**	**3.6**	**137 (10%)**
Yb-175	4.2	0.47 (87%)		396 (7%)
Lu-177g	**4.2**	**0.48 (78%)**	**1.7**	**208 (11%)**

Some examples: more recently studies

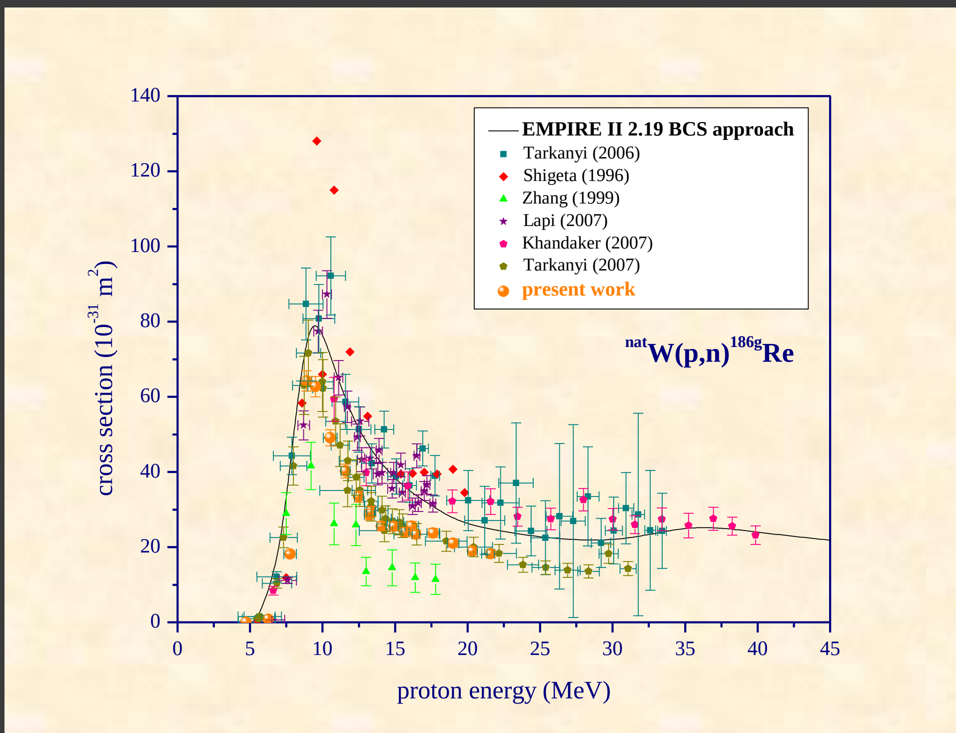
Measured cross sections in the range up to 19 MeV and set up of radiochemical separations for:

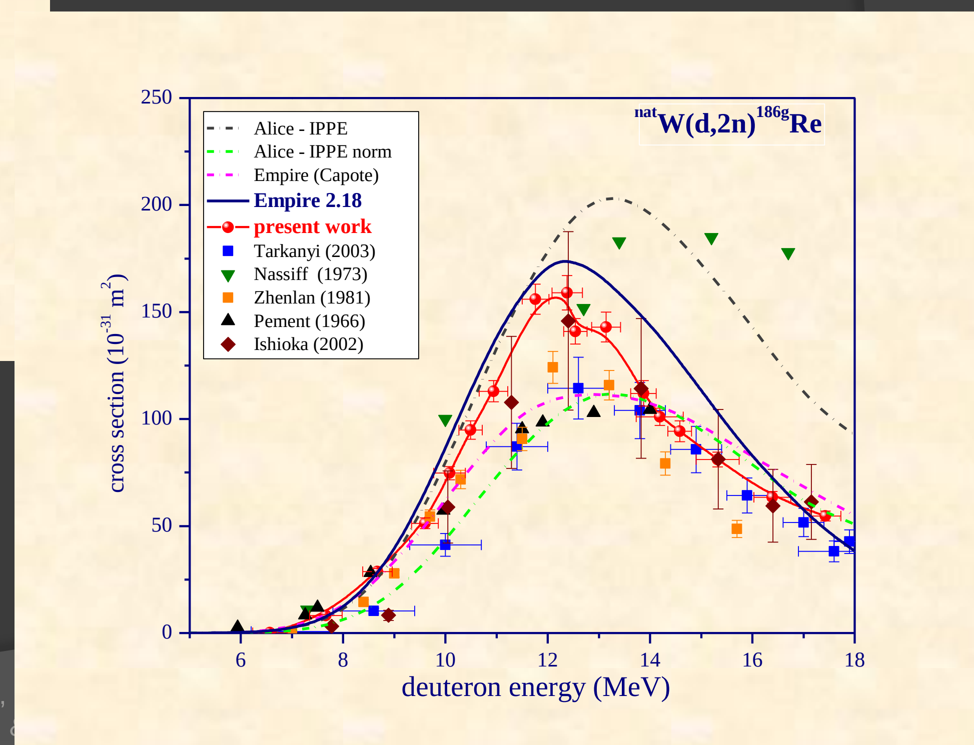
$^{186}W(d,2n)^{186g}Re$, $^{176}Yb(d,p)^{177g}Lu$

to be used in metabolic radiotherapy and for paliative treatment of bone metastasis pain.

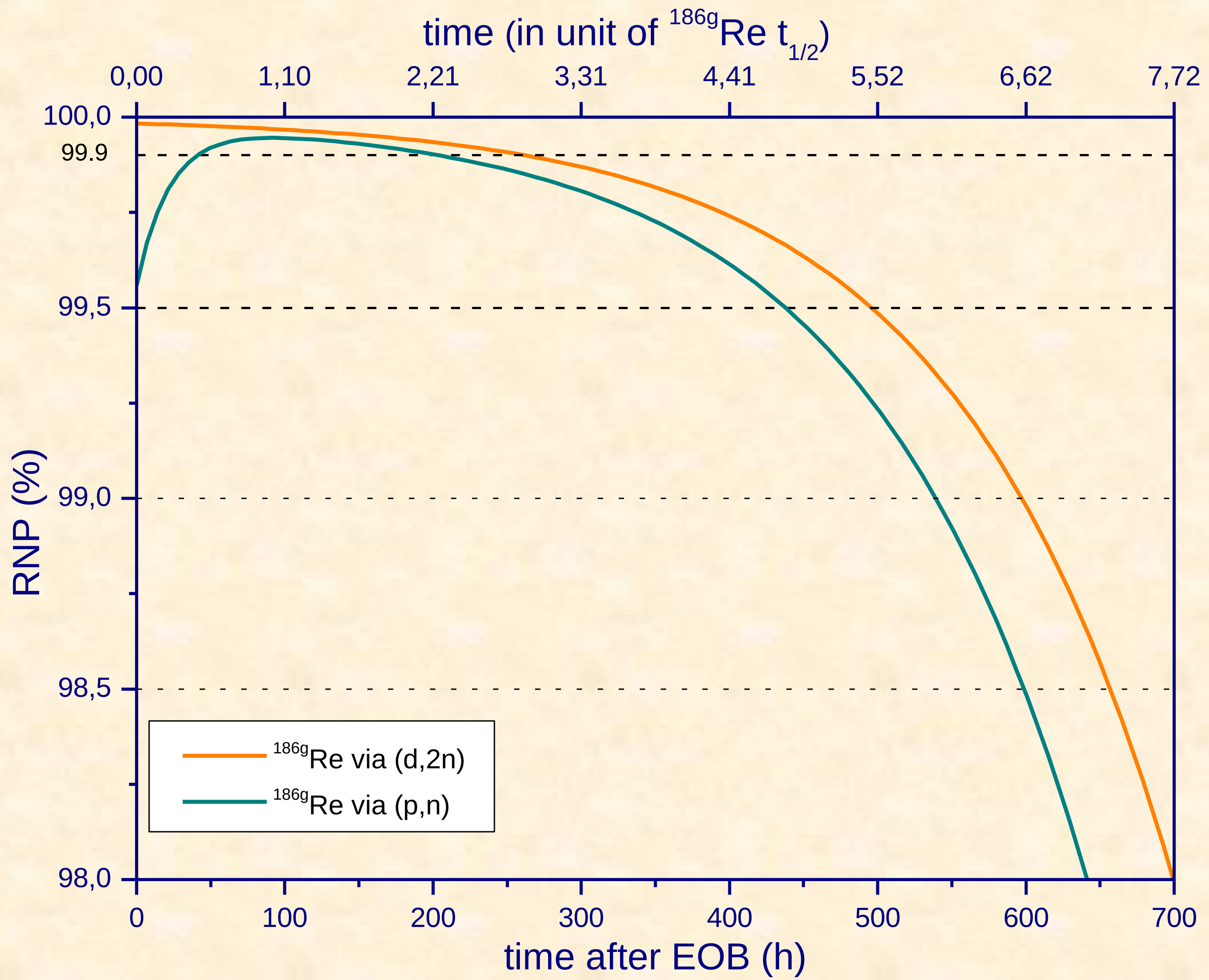


Comparison between cross sections for W(p,n)^{186g}Re and W(d,2n)^{186g}Re





Comparison of radionuclidic purity for different ^{186g}Re production methods on ^{186}W enriched target

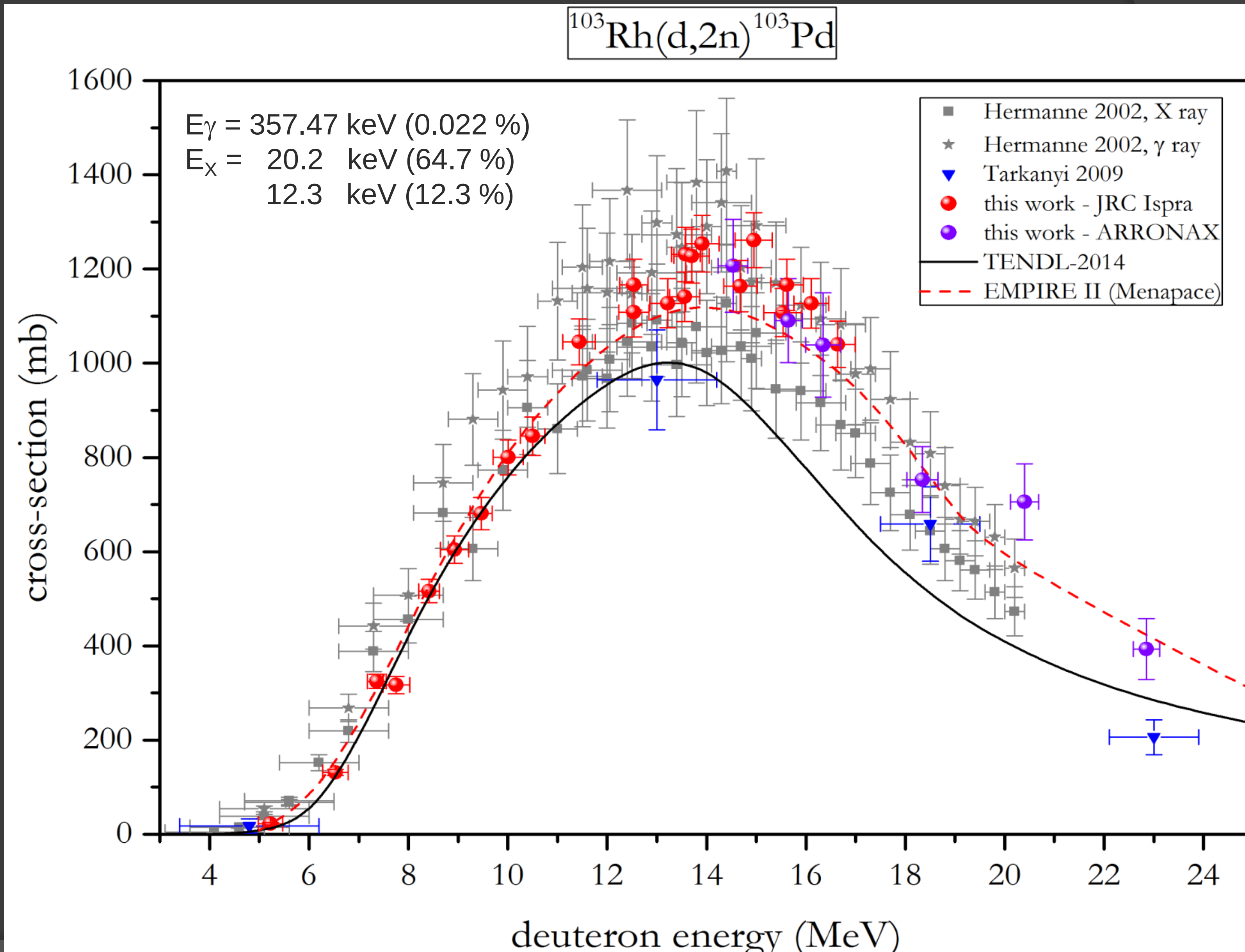


Future Programme
collaboration with ARRONAX, France

Often the (n,γ) reactions lead to non-sufficiently high specific activity (in CA form), thus alternative NCA methods are required.
Hot-atom recoil method (i.e. Szilard-Chalmers) is inefficient.

- ^{103}Rh (d,2n) ^{103}Pd NCA
  prostate brachytherapy (SS or Ti seeds)
- ^{89}Y (d,2n) ^{89}Zr NCA
  for PET and immuno-radiotherapy
- ^{110}Pd (d,2n) ^{111}Ag NCA
  silver nanospheres and metal chelates
- ^{198}Pt (d,2n) ^{199}Au NCA
  gold nanospheres and metal chelates

Cross Section of ^{103}Rh(d,2n)^{103}Pd ($t_{1/2}$ = 16.96 d)



For the future utilization of the new cyclotron at LNL

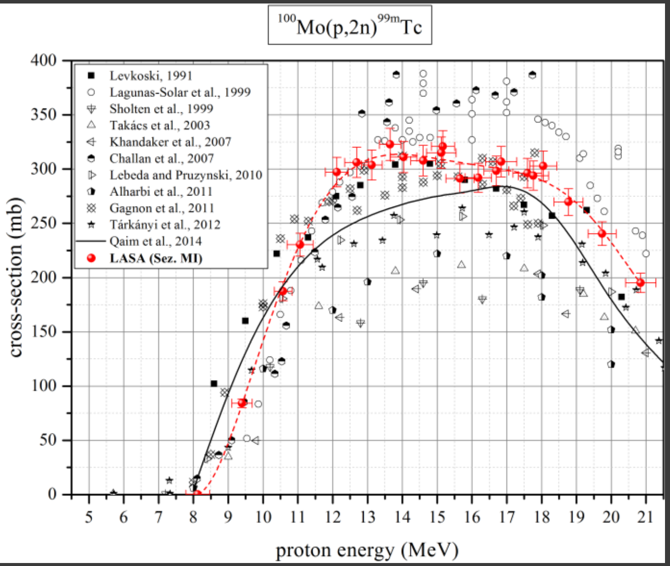
a) Experimental measurements of the cross sections for the different reaction channels for the ^{100}Mo(p,xn) nuclear reaction; determination of the Thick Target Yields to define the optimal irradiation conditions

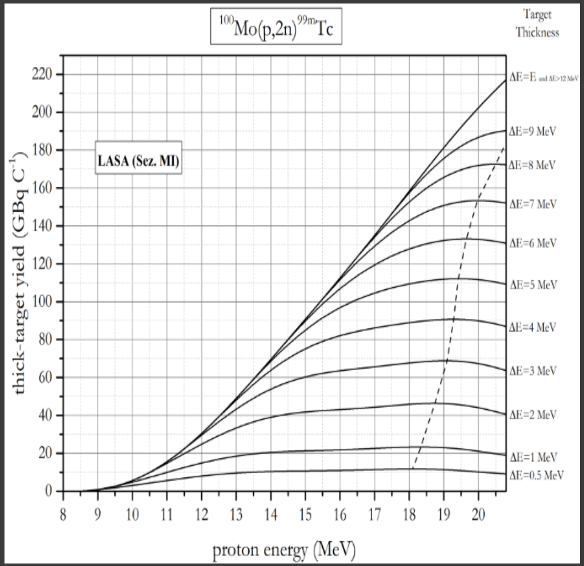
b) In collaboration with INFN-PV set up of the radiochemical separation of Tc from Mo target and interferences and the recovery of Mo

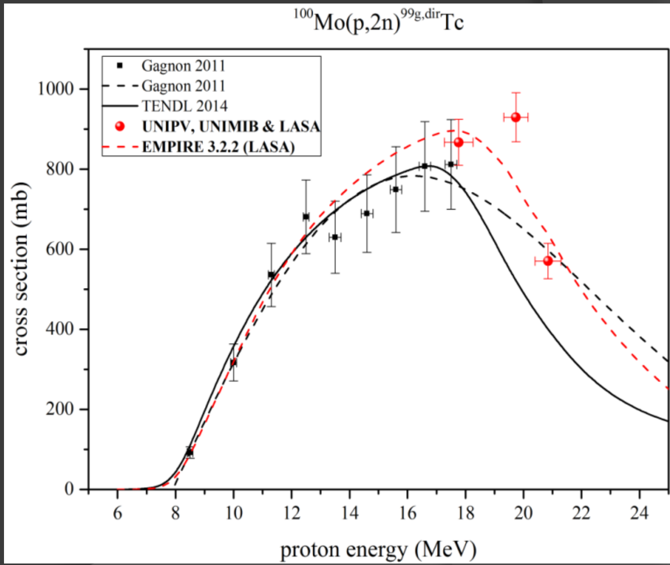
a) Cross Section of ^{100}Mo(p,2n)^{99m}Tc

a) Thick Target Yield of ^{100}Mo(p,2n)^{99m}Tc

b) Cross Section of ^{100}Mo(p,2n)^{99g,dir}Tc







S. MANENTI, U. HOLZWART, M. LORIGGIOLA, L. GINI, J. ESPOSITO, F. GROPPI, F. SIMONELLI, The excitation functions of Mo-100(p,x)Mo-99 and Mo-100(p,2n)Tc-99m, Applied Radiation and Isotopes. 94 (2014) 344

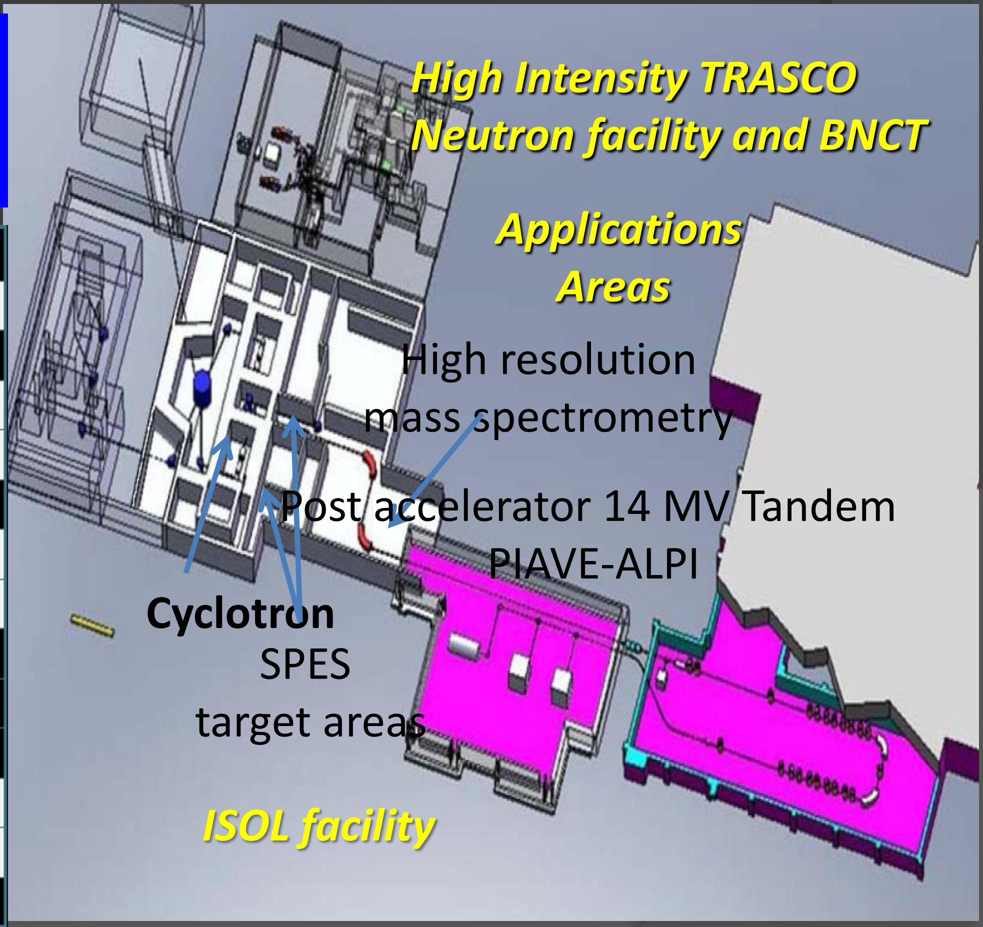
IAEA CRP project F22062 (Dec 2011 – Dec. 2015), INFN Research Activities Progress Report (as of June 2015) on Accelerator-based Alternatives to non-HEU Production of Mo-99/Tc-99m

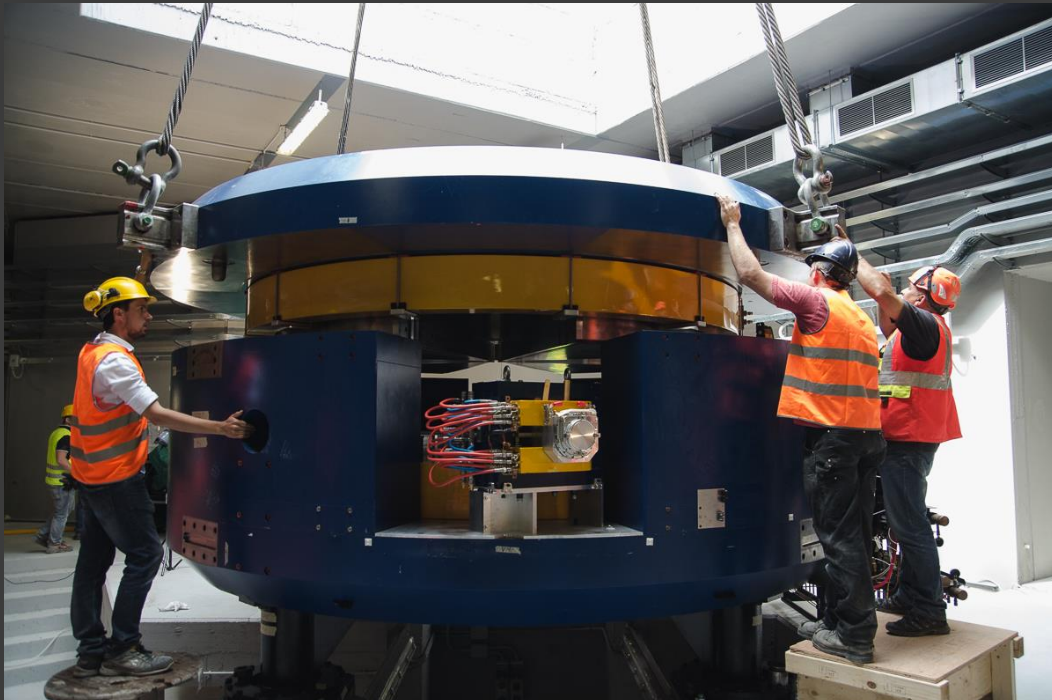
THE FUTURE
A CYCLOTRON ISOTOPE PRODUCTION CENTER FOR BIOMEDICAL RESEARCH
at INFN National Laboratory of Legnaro (PD)

Best Theratronics has been awarded a contract to construct a **70 MeV Cyclotron** for the INFN National Laboratory of Legnaro, Italy

Some proton-cyclotron isotope production
*(*enriched target)*
Possibility of twin target irradiation

radionuclide	target	reaction	p energy (MeV)	σ_{max} (mbar)
Cu-64	Ni	^{nat}Ni(p,n)	40	50
*Cu-64	Ni	^{64}Ni(p,n)	15	675
Cu-67	ZnO	^{68}Zn(p,2p)	70	25
Ge-68	Ga	^{69}Ga(p,2n)	45	100
*Ge-68	Ga	^{69}Ga(p,2p)	20	550
Sr-82	RbCl	^{nat}Rb(p,4n)	50	100
I-124	Te	^{nat}Te(p,n)	53	150
*I-124	Te	^{124}Te(p,n)	12	590
*Re-186	W	^{186}W(p,n)	10	17
Pd-103	Rh	^{103}Rh(p,n)	10	500
Th-228	Th	^{232}Th(p,X)	70	60
Ac-225	Th	^{232}Th(p,X)	60	3
Pa-230	Th	^{232}Th(p,3n)	30	260





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