CICLO DI SEMINARI

Artificial Intelligence in Medicine

Sapienza Università di Roma
Dip. Di Fisica - Aula Conversi
3 dicembre 2018

14:15 Introduction
Riccardo Faccini *(Sapienza e INFN Roma)*

14:35 Medical image processing and analysis
Alessandra Retico (INFN Pisa)

15:15 Artificial intelligence in MR image analysis
Carlo Mancini Terracciano (INFN Roma)

15:35 Break

15:55 Automatic classification of patients response to chemo-radiotherapy in rectal cancer
Cecilia Voena (INFN ROMA)

16:15 In vivo drugs monitoring by 19F-MR imaging and 19F-MR spectroscopy
Silvia Capuani (CNR ISC UOS Roma Sapienza)

16:35 Machine Learning applications to doctor-patient interactions
A. Ciardiello (Univ.Sapienza-INFN Roma)

https://agenda.infn.it/conferenceDisplay.py?confId=16961

INFN Istituto Nazionale di Fisica Nucleare
SAPIENZA UNIVERSITÀ DI ROMA

ARPG

SAPIENZA UNIVERSITÀ DI ROMA

INFN Istituto Nazionale di Fisica Nucleare

CENTRO FERMI Museo Storico della Fisica e Centro Studi e Ricerche Enrico Fermi

NUCLEAR MEDICINE

CHIRONE
(Radio Guided Surgery)

HADRON THERAPY

FOOT
(RBE in PT)

FRED
(TPS with GPU)

DOSE PROFILER
(Particle Therapy dosimetry)

MONDO
(Fast Neutron Detection)

GENIALE
(Low Energy Nuclear Interactions)

ARTIFICIAL INTELLIGENCE IN MEDICINE

MARIANNE
(Imaging for stadiation)

NEPTUNE
(19F-MRI)

FILOBLU
(Patient-Doctor interactions)

http://arpg-serv.ing2.uniroma1.it/arpg-site/index.php

Collaborations

Activity driven by medical input, with involvement of SMEs

POLITECNICO MILANO

FONDAZIONE BRUNO KESSLER

HIT Heidelberger Ionenstrahl-Therapiezentrum

FONDAZIONE I.R.C.C.S. ISTITUTO NEUROLOGICO CARLO BESTA

NUCLEOMED

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA Azienda Ospedaliera di Reggio Emilia Arcispedale S. Maria Nuova

fondazione CNAO

GSI

ISTITVTO SVPERIORE DI SANITÀ

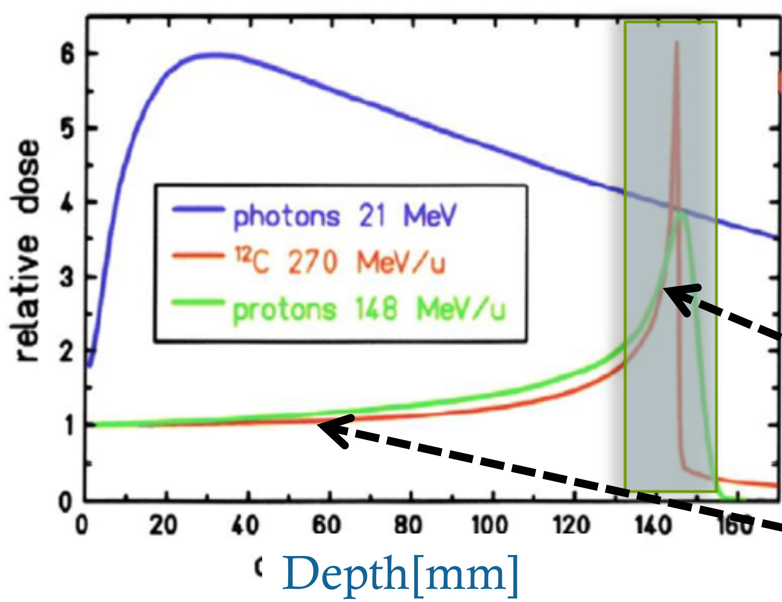
Gemelli

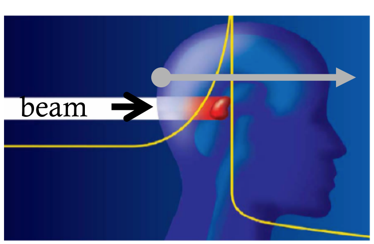
Istituto Europeo di Oncologia

HADROTHERAPY

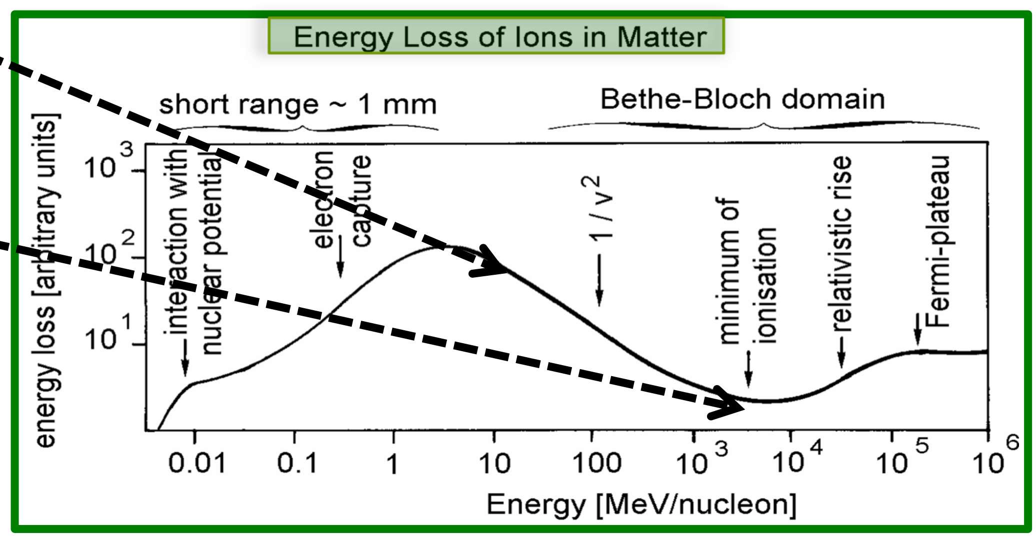
Hadrotherapy

Proton/ion beams on patient





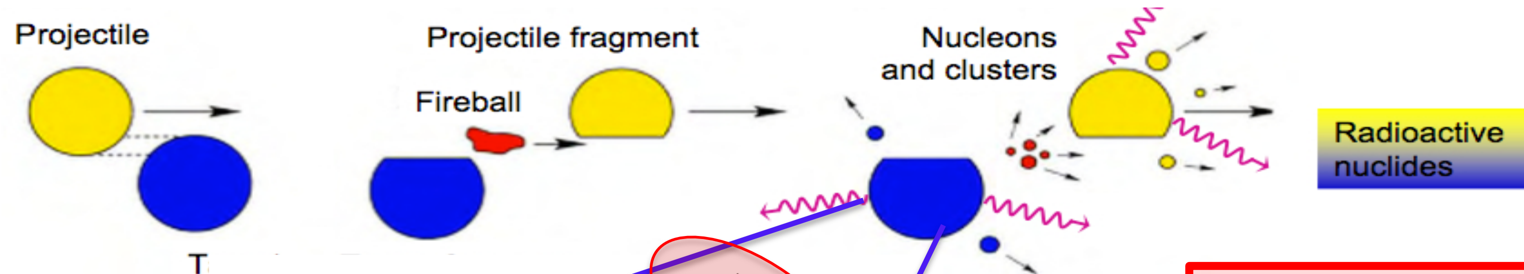
Concentrate release of energy inside tumor due to release of energy in ionization.



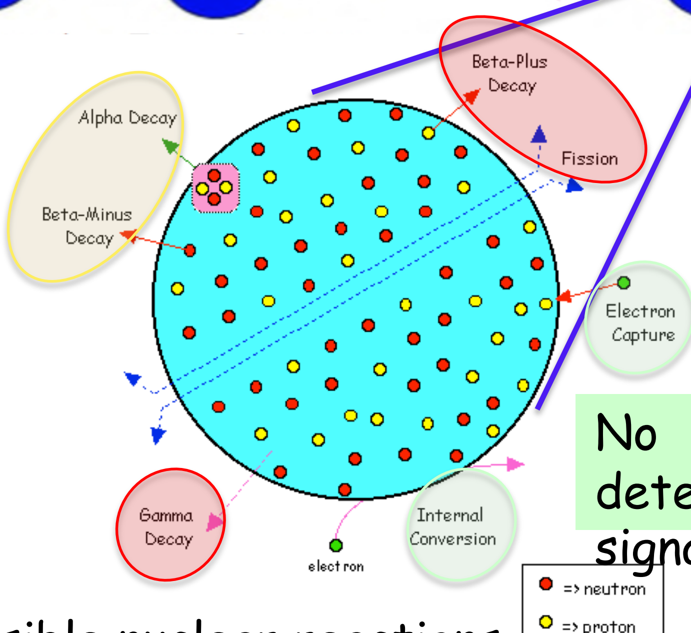
Measuring the dose

RF, V. Patera, "Dose Monitoring in Particle Therapy", Mod. Phys. Lett. A

Based on nuclear reactions between the projectile and the patient



Don't exit patient



No detectable signal

Possible nuclear reactions

Reactions of interest

- β+ decays
- Prompt γ
- Charged products

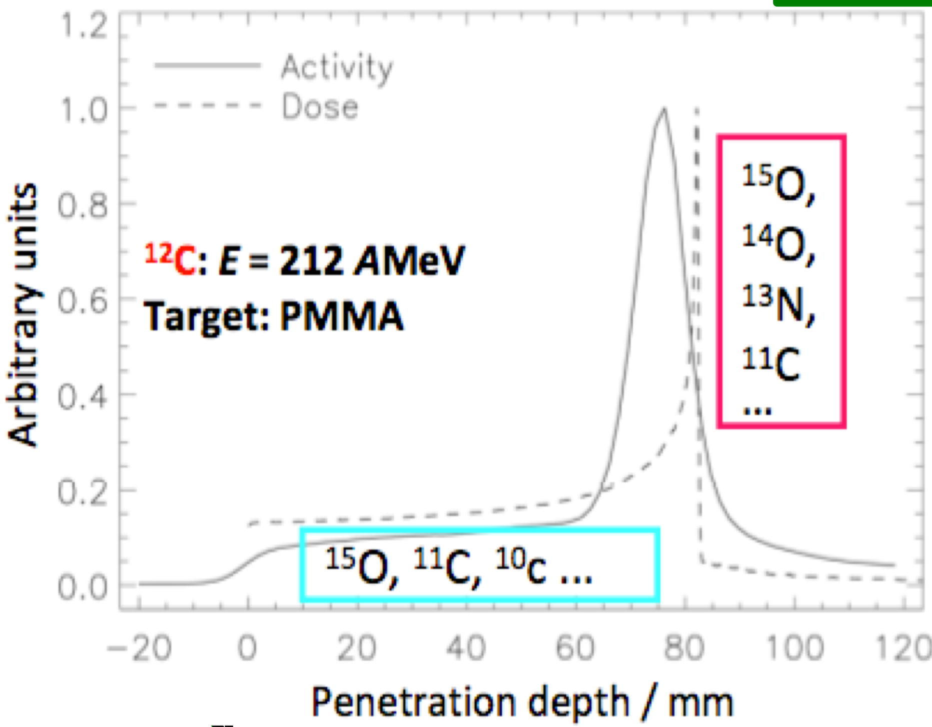
Correlation between activity and dose

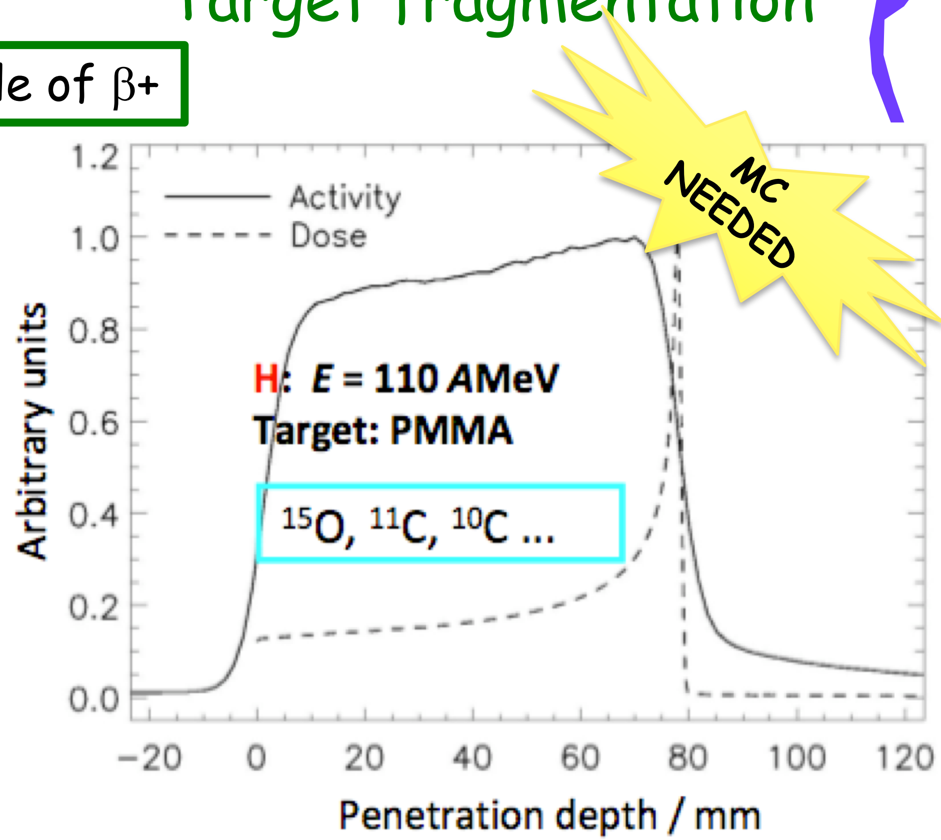
Therapy beam	^{1}H	^{3}He	^{7}Li	^{12}C	^{16}O	Nuclear medicine
Activity density / Bq cm^{-3} Gy^{-1}	6600	5300	3060	1600	1030	$10^4 - 10^5$ Bq cm^{-3}

Projectiles & target fragmentation

Example of β+

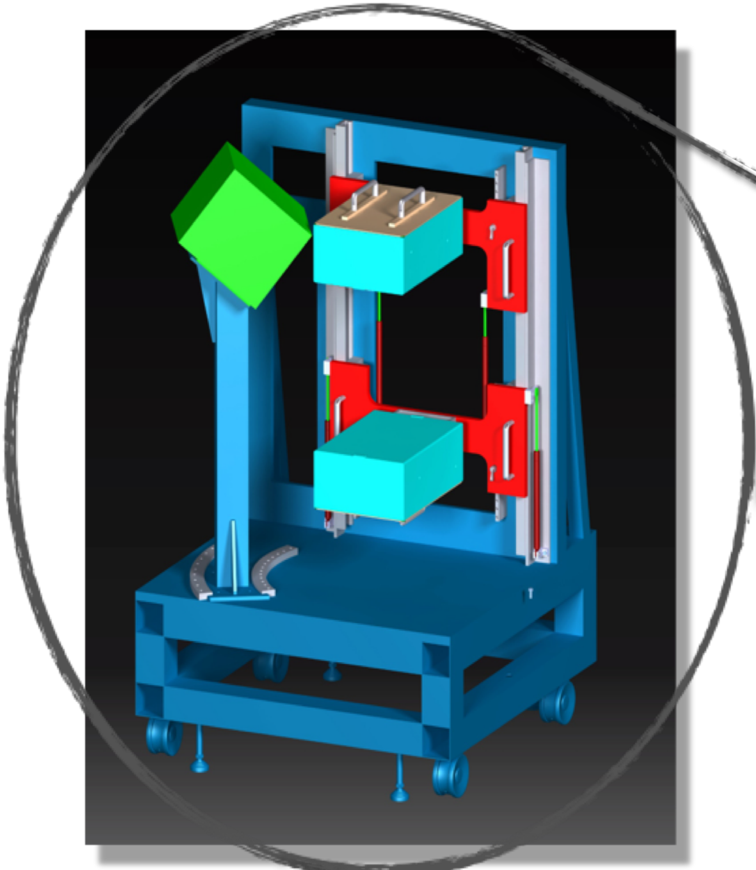
Target fragmentation

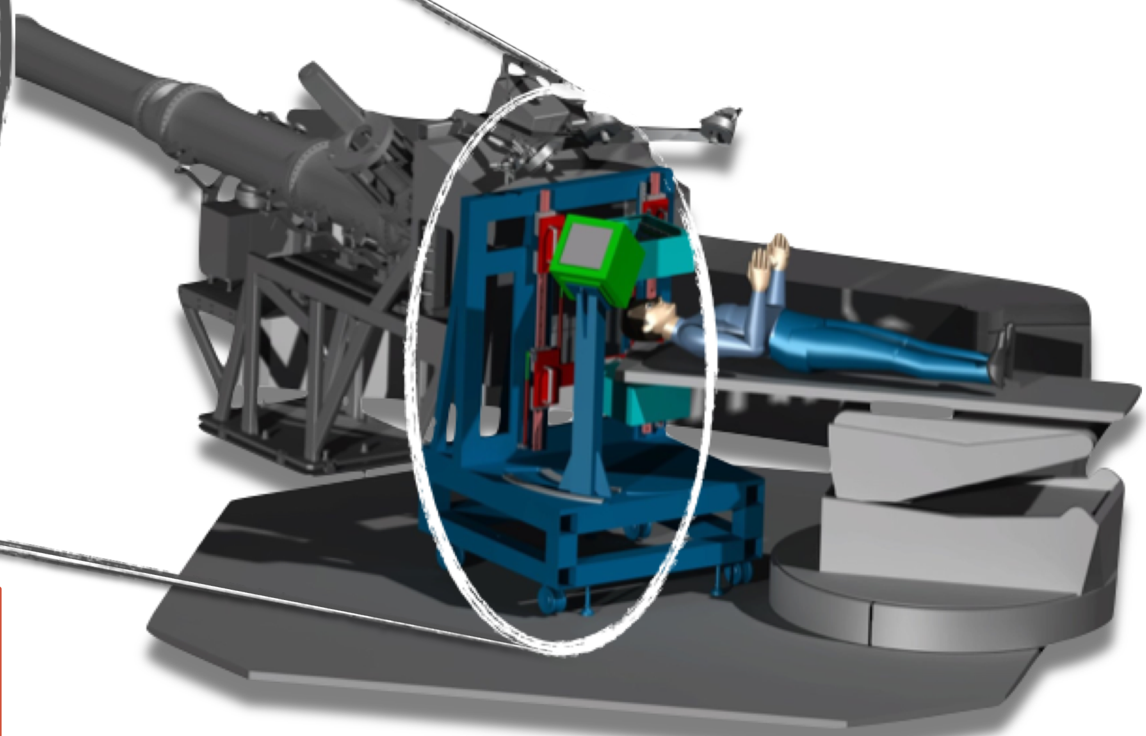




Range monitor applications

- To exploit the secondary particles detections as an online monitor, a Dose Profiler has been designed (within the INSIDE Italian project) to be deployed in the CNAO treatment center.





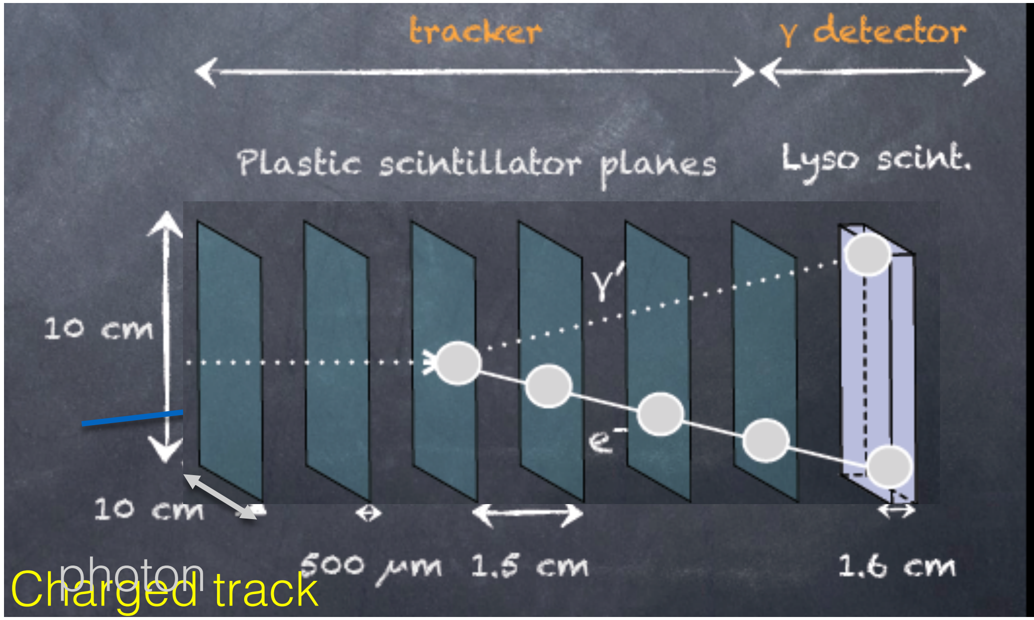
Project funded as a part of **INSIDE Prin**, **INFN RDH** and **Premiale** C.F.

Dose Profiler

Need a detector to simultaneously measure the rate of:

- charged particles with multilayer for track reconstruction

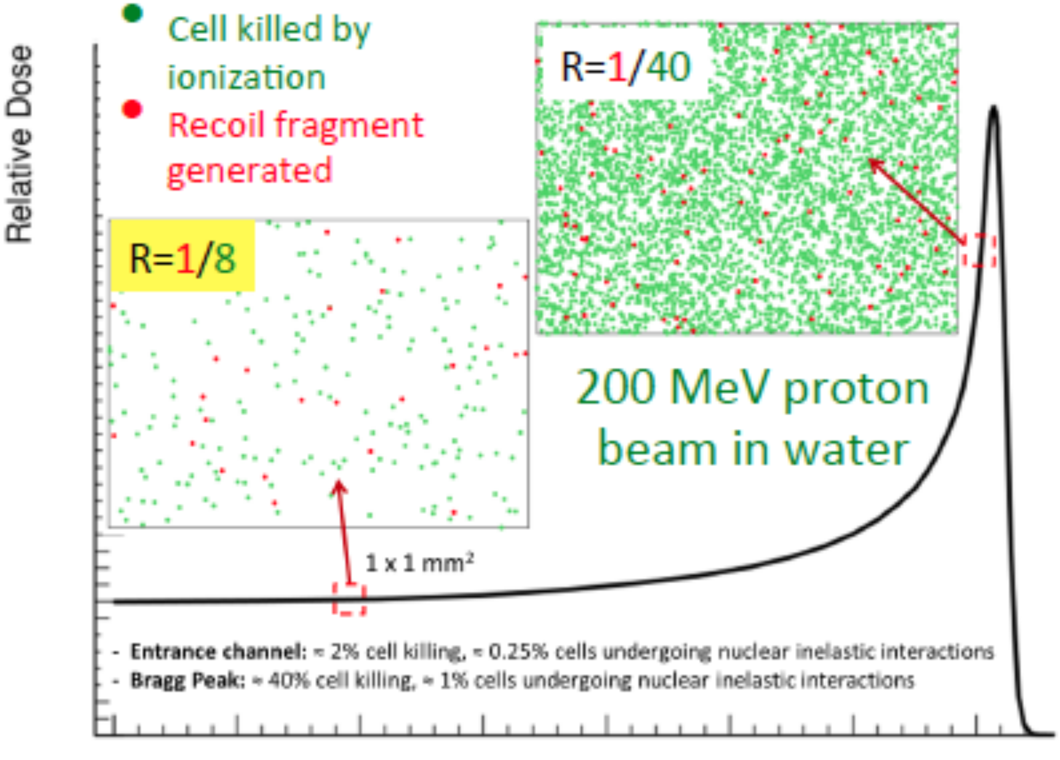
- single photons with compton camera



FOOT (RBE in PT)

Target (patient) fragmentation & PT

Target fragmentation in proton therapy: gives contribution also outside the tumor region!



Cancers 2015,7 Tommasino & Durante

About 10% of biological effect in the entrance channel due to secondary fragments (Grun 2013)

Largest contributions of recoil fragments expected from

He, C, Be, O, N

In particular on Normal Tissue Complication Probability

See also :

- Paganetti 2002 PMB
- Grassberger 2011 PMB

p-> C, p->O scattering @200 MeV

The elastic interaction and the forward Z=1 fragment production (p,d,t) are quite well known. Large uncertainty on large angle Z=1,2 fragments.

Missing data on heavy fragments. Unreliable nuclear models

"Heavy" (A>4) fragment yields and emission energy ~ unknown

Very low energy-short range fragments.

MCs confirm this picture

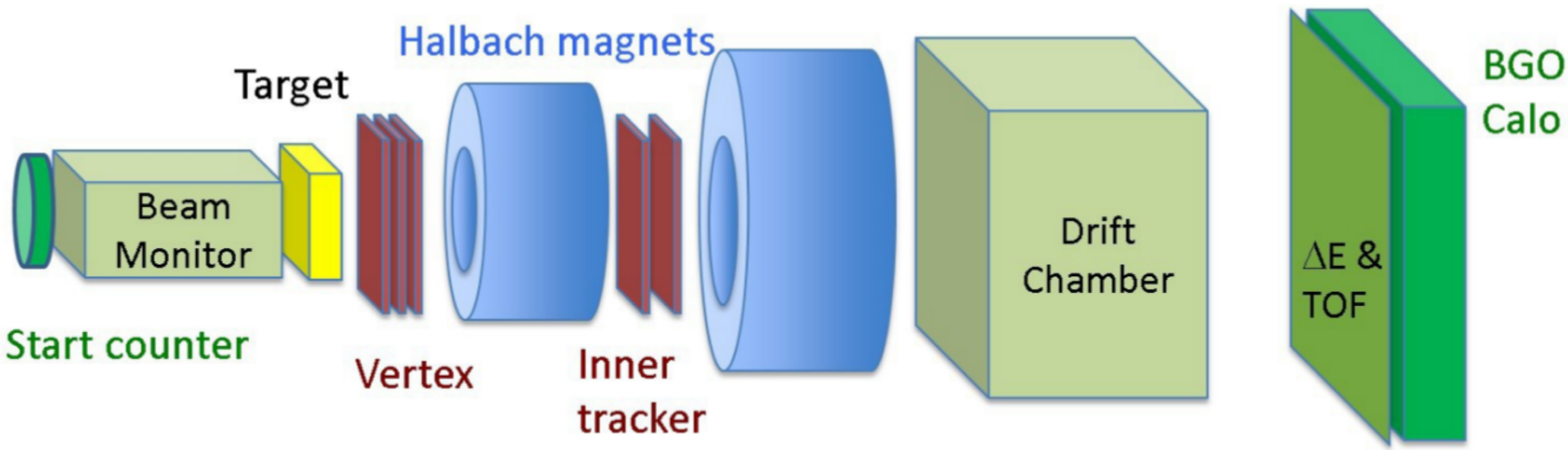
Nuclear model & MC not reliable

Analitic model results on p->O @200 MeV

Fragment	E (MeV)	LET (keV/μm)	Range (μm)
^{15}O	1.0	983	2.3
^{15}N	1.0	925	2.5
^{14}N	2.0	1137	3.6
^{13}C	3.0	951	5.4
^{12}C	3.8	912	6.2
^{11}C	4.6	878	7.0
^{10}B	5.4	643	9.9
^{8}Be	6.4	400	15.7
^{6}Li	6.8	215	26.7
^{4}He	6.0	77	48.5
^{3}He	4.7	89	38.8
^{2}H	2.5	14	68.9

Cancers 2015,7 Tommasino & Durante

The FOOT Experimental setup

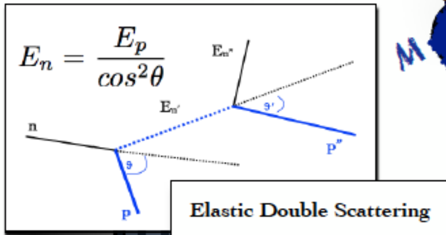


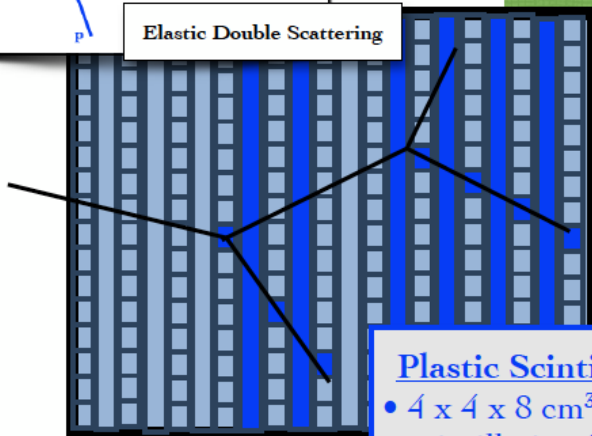
Expected performances:

- Resolution on fragment X-section < 5%
- Energy resolution < 1 MeV/u
- Measurements of Z with mistag <3%
- Measurement of A with mistag < 5%

MONDO (Fast Neutron Detection)

High energy neutron detector





In a particle therapy treatment the beam interactions with patient produce many secondary particles. Monitoring methods using photons and charged particles have already been proposed, but no attempt has been made yet to use the abundant neutron component. The large penetrating power of neutrons produces nearly energy threshold free escape, providing a secondary particle sample that is higher in number with respect to photons and charged particles. Therefore, neutrons allow for a backtracking of the emission point that is not affected by multiple scattering.

Moreover The neutron induced complications are the main concerns in Particle Therapy administration and planning, in particular in pediatric treatments [1].

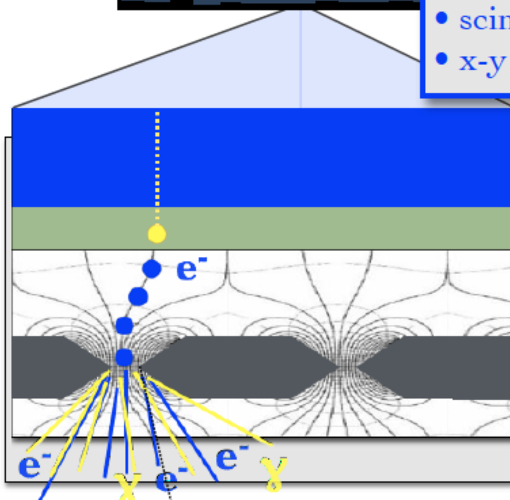
We want to measure and track the ultra-fast neutrons produced in Particle Therapy treatments developing a **tracking device** tailored for hadrontherapy dose monitoring applications!

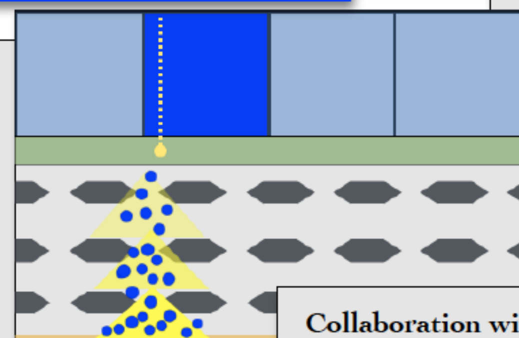
[1] M.Durante W.D. Newhauser doi:10.1038/nrc3069

Plastic Scintillator

- $4 \times 4 \times 8$ cm^3;
- scintillating fibres 250 μm;
- x-y layer orientation;

Image Intensifier: Triple GEM detector





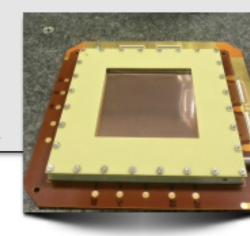
Collaboration with CERN

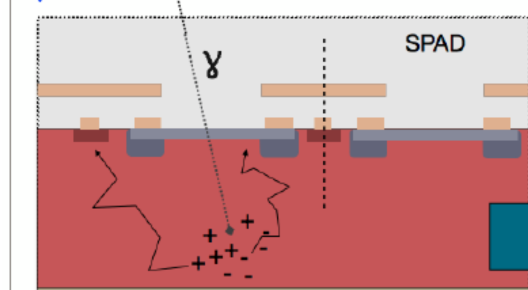
Gas Electron Multiplier

- 45 μm hole
- 70 μm hole distance
- triple GEM

We use GEM as photon intensifier instead of look for electron multiplication

For GEM light measurements => See also D.Pinci POSTER





- ☑ integrated TDC (resolution ~65 ps)
- ☑ self triggered sensor
- ☑ pixel 600 μm

Signals ReadOut: CMOS Single Photon Avalanche Diode (SPAD) array sensor

GENIALE
(Low Energy Nuclear Interactions)

- Despite the numerous and relevant application would use it, there is no dedicated model to nuclear interaction below 100 MeV/A in Geant4

- Many papers showed the difficulties of Geant4 in this energy domain:

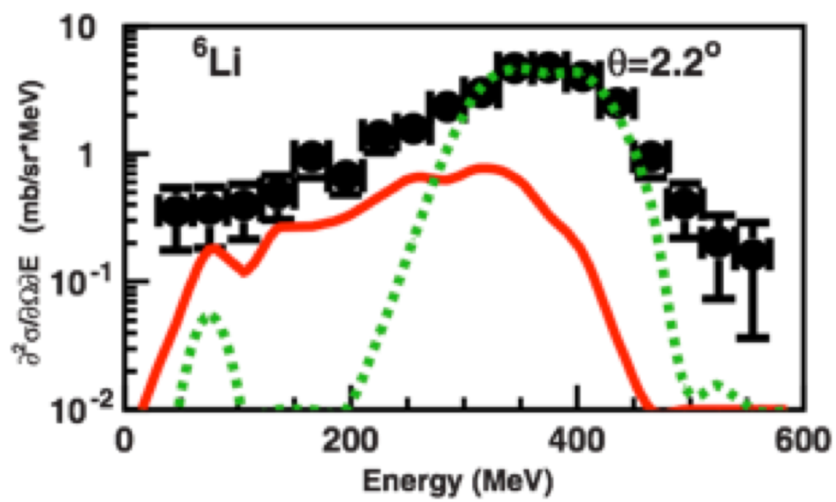
  - Braunn et al. have shown discrepancies up to one order of magnitude in ^{12}C fragmentation at 95 MeV/A on thick PMMA target

  - De Napoli et al. showed discrepancy specially on angular distribution of the secondaries emitted in the interaction of 62 MeV/A ^{12}C on thin carbon target

  - Dudouet et al. found similar results with a 95 MeV/A ^{12}C beam on H, C, O, Al and Ti targets

- **Exp. data**
- **G4-BIC**
- **G4-QMD**

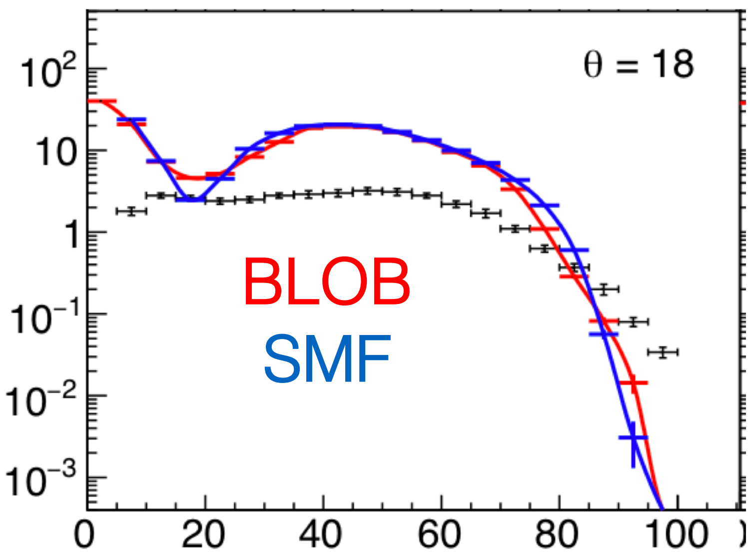
[Plot from De Napoli et al. Phys. Med. Biol., vol. 57, no. 22, pp. 7651–7671, Nov. 2012]



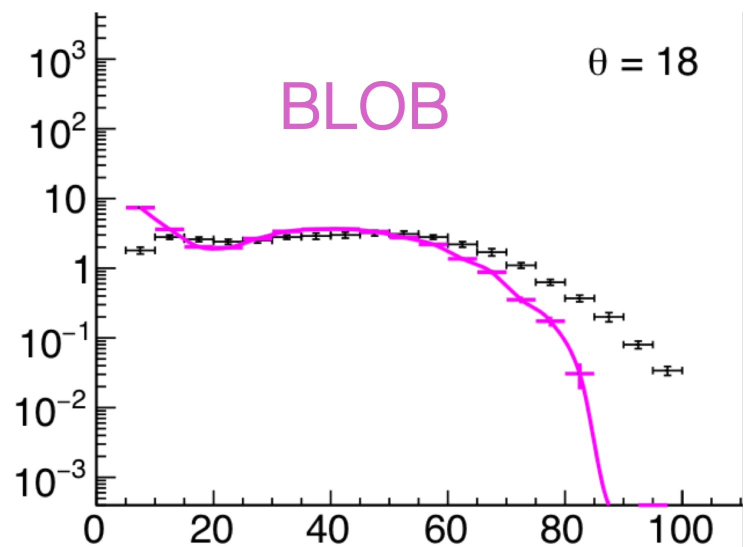
Cross section of the ^{6}Li production at 2.2 degree in a ^{12}C on ^{nat}C reaction at 62 MeV/A.

GENIALE: results

Example: alpha production



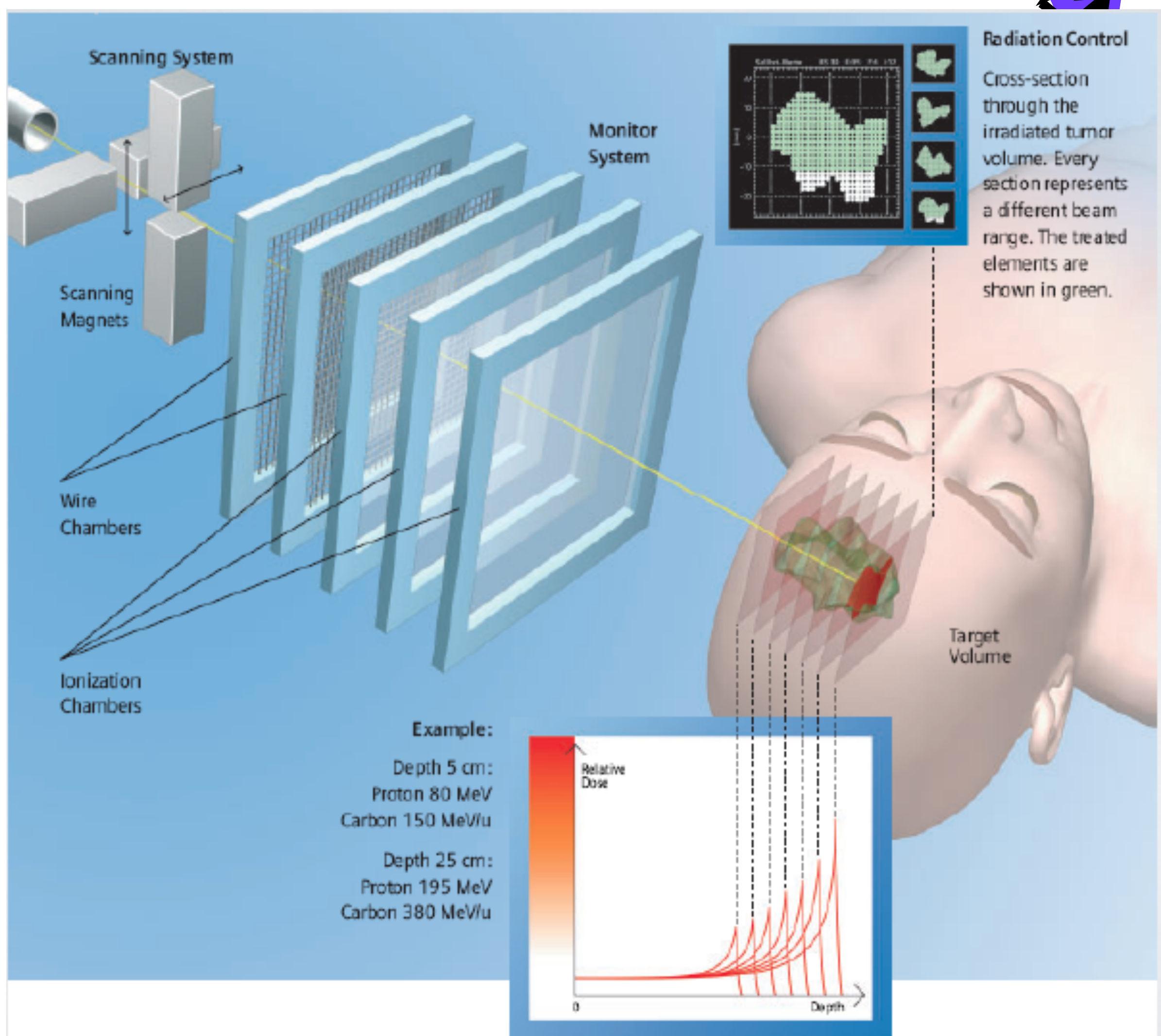
- COALESCENCE
- EXITATION ENERGY CORRECTION



FRED
(TPS with GPU)

Treatment Planning System

From the tumor margin to the beam sequencing ("Raster Scan")



Use of GPUs

Typical times:

- Full MC 72hr
- Analytical commercial sw: 1hr
- GPUs → 1min

Algorithm 3.2.1 Original Dose Calculation

for $i = 0$ to N_{beams} **do**
  for $j = 0$ to $N_{beamlets}[i]$ **do**
    $currentBeamlet \leftarrow j + ptr$
    calculate angle θ
    calculate radiological depth d
    compute input and output body points and corrections W_1,W_2
    for $ivoxel = 0$ to N_{voxels} **do**
      calculate parameters to dose calculation
      compute F_x
      calculate dose $D(\vec{r})$
    end for
  end for
  $ptr \leftarrow ptr + N_{beamlets}[i]$
end for

Split algo to parallelize

Algorithm 3.2.2 Loop 1

for $i = 0$ to N_{beams} **do**
  for $j = 0$ to $N_{beamlets}[i]$ **do**
    $currentBeamlet \leftarrow j + ptr$
    calculate and store angle θ
    calculate and store radiological depth d
    compute and store input and output body points
  end for
  $ptr \leftarrow ptr + N_{beamlets}[i]$
end for

Algorithm 3.2.4 Kernel Loop

threadIdx, blockIdx
for $i = 0$ to N_{beams} **do**
  for $j = 0$ to $N_{beamlets}[i]$ **do**
    calculate x and y
    calculate parameters to dose calculation
    compute F_x
    each thread calculates its dose contribution $D(\vec{r})$
  end for
  $ptr \leftarrow ptr + N_{beamlets}[i]$
end for

Hardware and Performance

		Threads	primary/s	$\mu s/primary$
CPU[a]	full-MC *	1	0.75 k	1340
	FRED	1	15 k	68
	FRED	16	50 k	20
	FRED	32	80 k	12.5
GPU	FRED	1 GPU[1]	500 k	2
	FRED	2 GPU[2]	2000 k	0.5
	FRED	4 GPU[3]	20000 k	0.05

Table A1: Computing times for different hardware architectures.

[a] motherboard with two Intel® Xeon E5-2687 8-Core CPU at 3,1GHz

[1] LAPTOP: Apple® MacBook Pro with one AMD® Radeon R9 M370X.

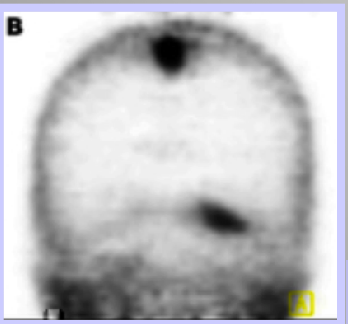
[2] DESKTOP: Apple® Mac Pro with two AMD® FirePro D300.

[3] WORKSTATION: Linux box with four NVIDIA® GTX 980.

* FLUKA or Geant4

NUCLEAR MEDICINE

Radio Guided Surgery



PET/SPECT scan to estimate receptivity and background

Each tumor requires its own tracer

Administration of radio-tracer

During surgery a probe is used to detect residuals/lymphnodes

Probe adjustable to needs

LIMITS OF γ-RGS

140 keV photons

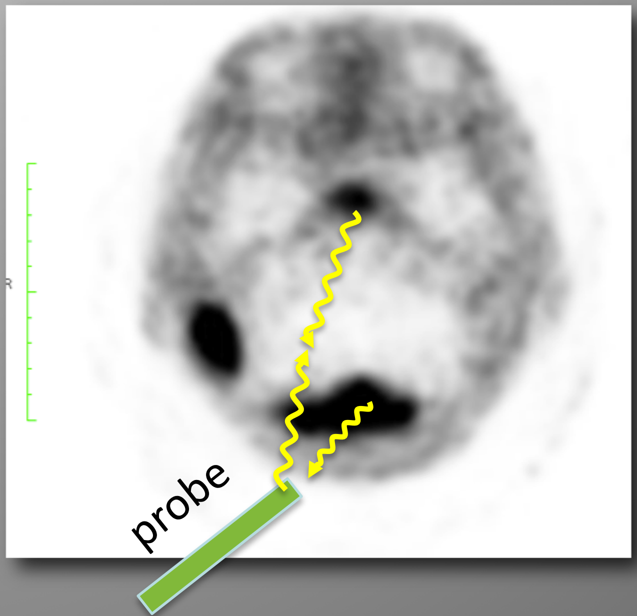
➔ attenuation in body ~8cm

Long range of gamma's involve:

- exposure of medical personnel
- Background from healthy organs

Difficult to apply in:

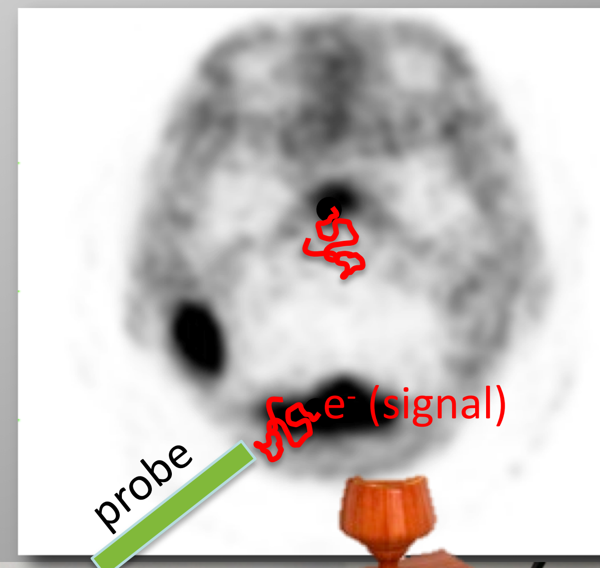
- Brain tumors
- Abdominal tumors
- Pediatric tumors



A CHANGE IN PARADIGM

E. Solfaroli Camillocci et al, Sci. Repts. 4,4401 (2014)

- Use of β^- tracers (electrons): pros
  - Detect electrons that travel ~100 times less than γ
  - Tracers with ^{90}Y can be used (already used for Molecular RT)
  - No background from gamma
    - Shorter time to have a response
      - Smaller administered activity
    - Smaller and more versatile detector
    - reduced effect of nearby healthy tissues
    - Reduced dose to medical staff



NOTE: only detection at contact is possible

EXTEND RGS TO MORE CLINICAL CASES

The probe prototype

Compact, easy to handle, local measurement

Simple technology:
- scintillating crystal
- Light sensor (SiPM)

Most stringent constraints:
- Mechanics
- electrical safety
- sterilization

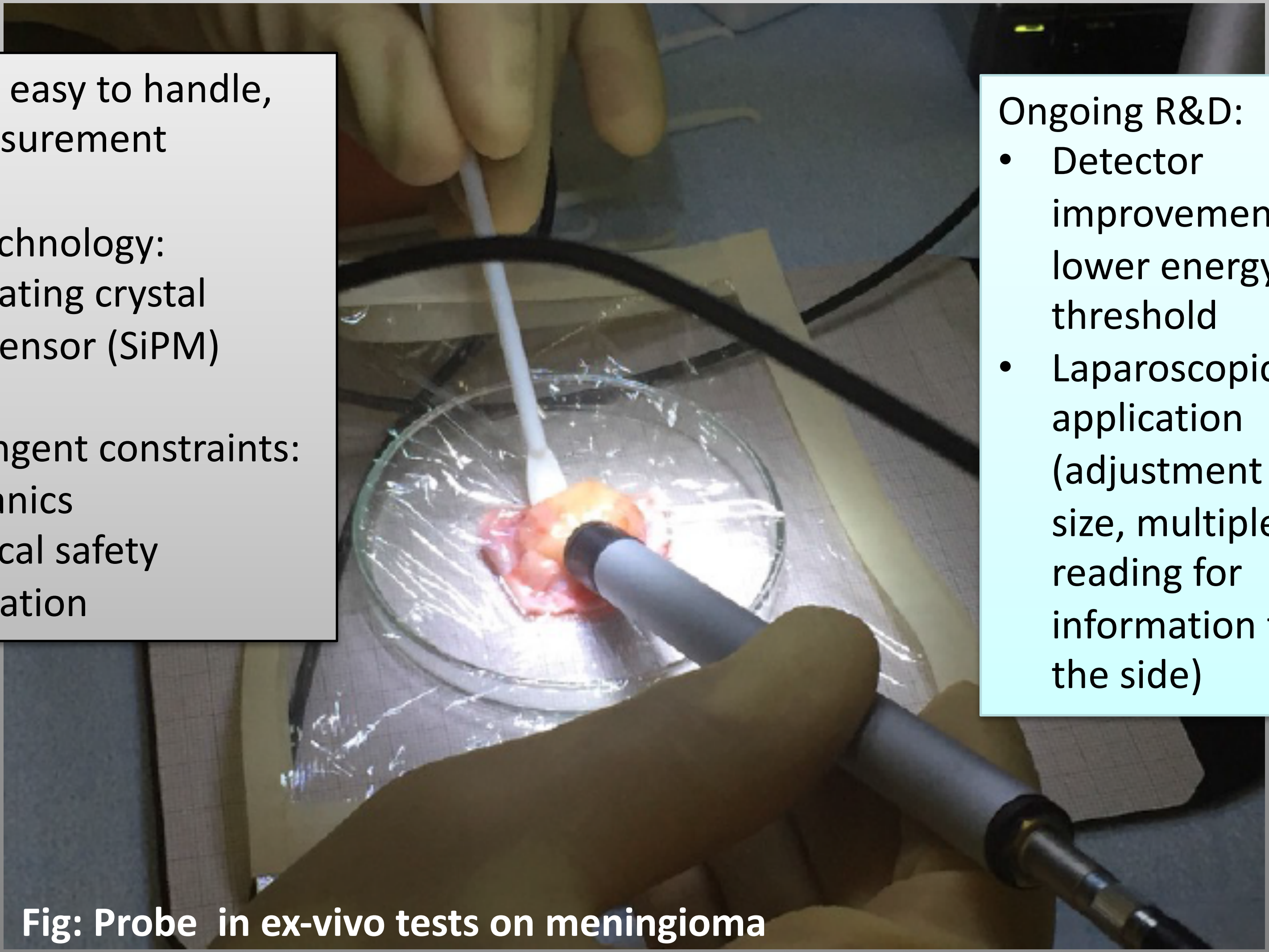
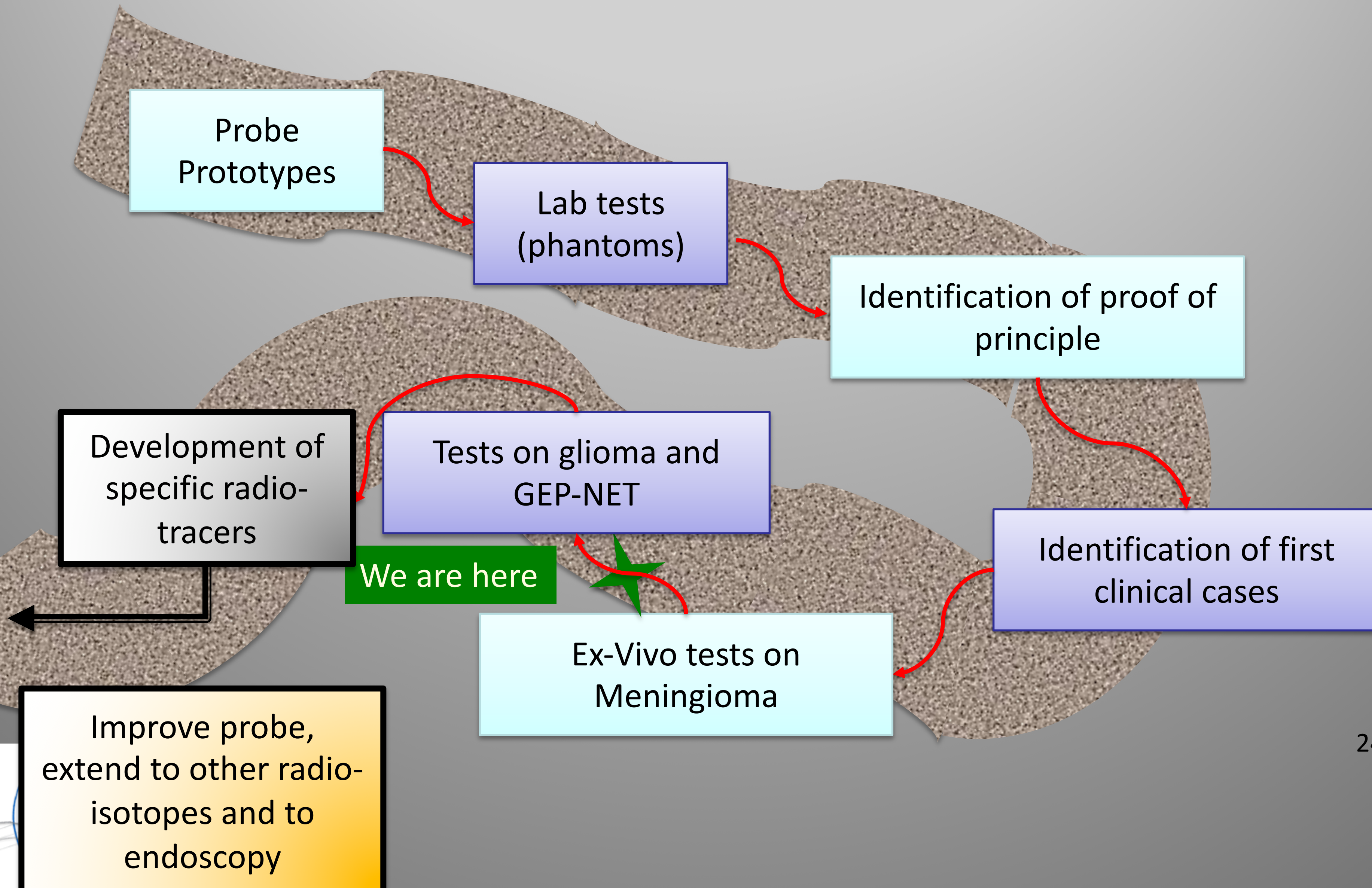


Fig: Probe in ex-vivo tests on meningioma

Ongoing R&D:
- Detector improvements to lower energy threshold
- Laparoscopic application (adjustment in size, multiple reading for information from the side)

RESEARCH PATH



Perspectives

Application to other radio-tracers

- ^{68}Ga in prostate cancer
- Development of a CMOS sensor based device
  - Extend to more radionuclides→ more tumors

Other applications of low energy electrons detection

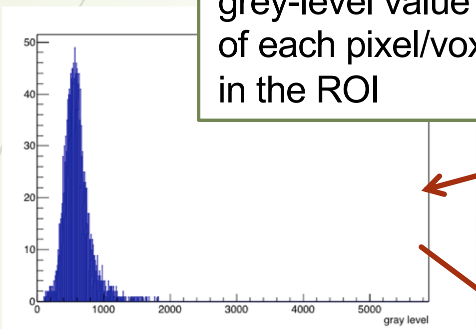
- dosimetry in **radio-methabolic therapy**
- use of cell-phones in **massive dose monitoring** during nuclear emergencies
- particulate density measurement in **pollution detectors**

ARTIFICIAL INTELLIGENCE IN MEDICINE

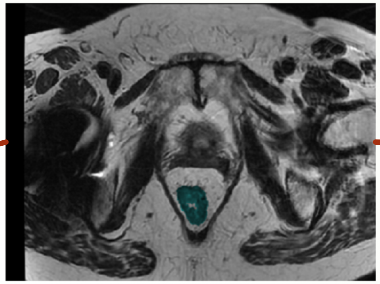
MARIANNE
(Imaging for stadiation)

→ Talks by Carlo Mancini Terracciano and Cecilia Voena

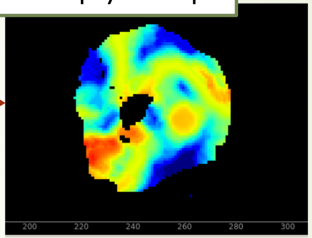
Automatic classification of response to chemoradiotherapy in rectal cancer using 3T T2-w MRI



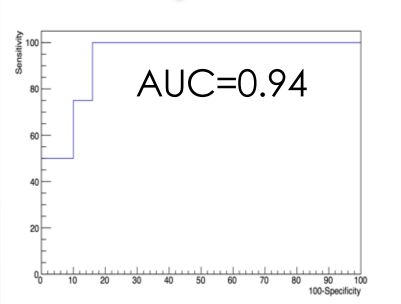
grey-level value of each pixel/voxel in the ROI



Entropy map



Machine learning algorithm: Random Forest classificator to stratify patient respnce



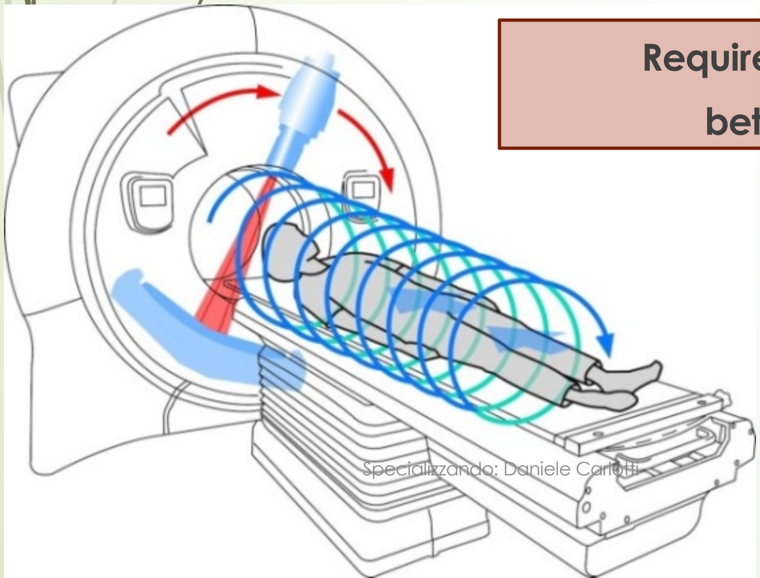
S. Ciardiello, RF, R. Paramatti, C. Mancini Terracciano, C. Voena, et al …

Avoid surgery to 50% of patients that would not need it

Paper to be submitted to Radiology

Texture analysis of MR images

Tomotherapy Quality assurance



Tomotherapy (radiotherapy by slices) is a radiotherapy with very accurate dose profiling

↓

Complex dose delivery

↓

Requires accurate verification of correspondence between estimated and measured activity

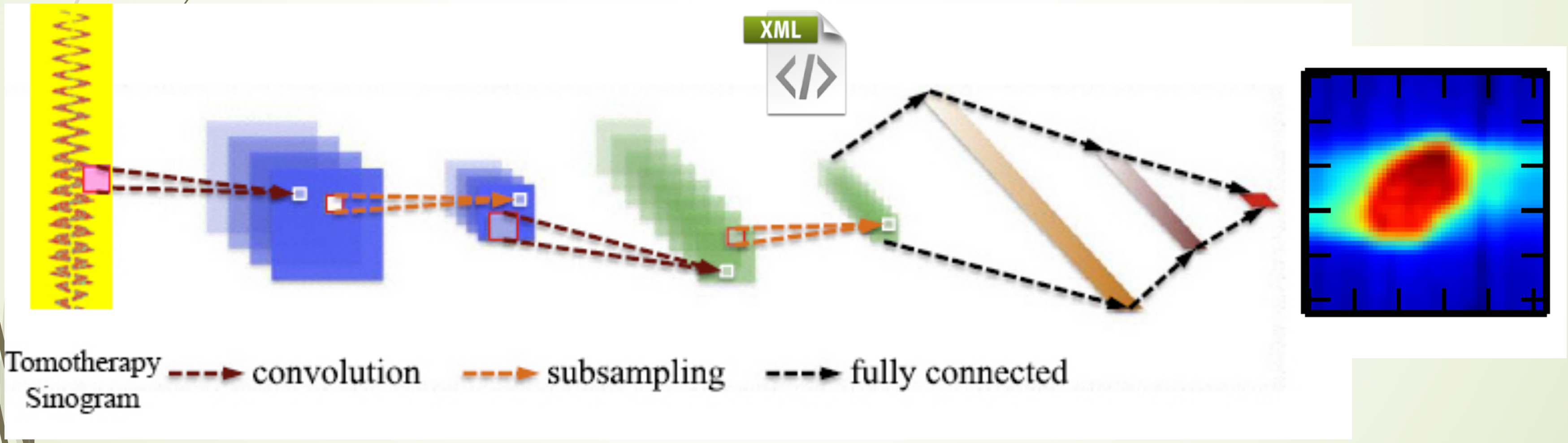
Application of Machine Learning

Aim of the study: develop an algorithm capable to estimate, patient by patient, the dose profile of TomoTherapy HiArt Delivery Quality Assurance (DQA)

Towards artificial QA

Raw Data

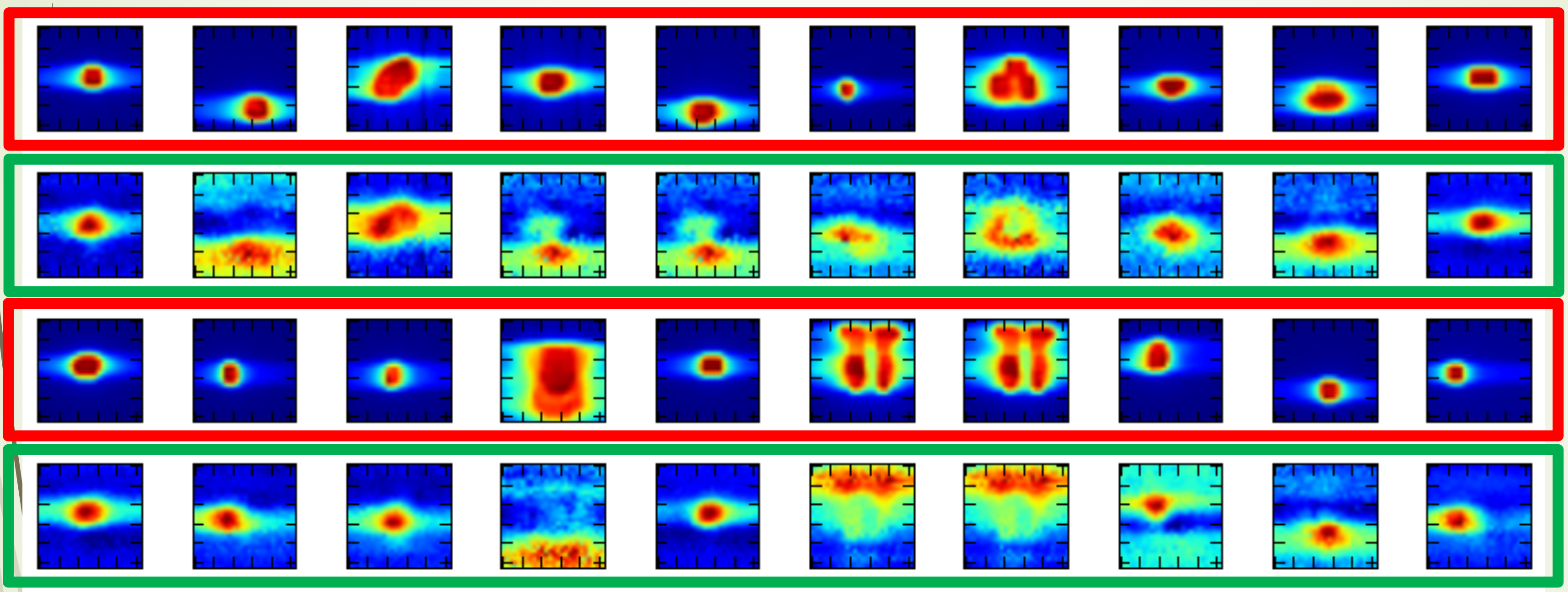
Dose profile



USE OF NNETS

Specializzando: Daniele Carlotti

Virtual dose distribution



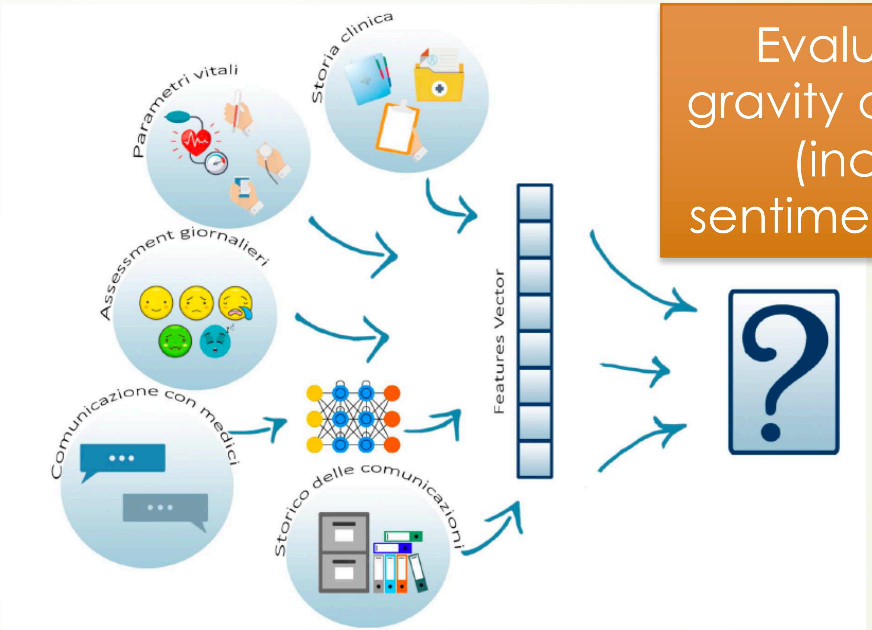
- In **red** measured images (sample of 729)
- In **gree** images simulated with the developed neural network.

FILOBLU
(Patient-Doctor interactions)

→ Talk by Andrea Ciardiello

Machine learning for patient–doctor interactions

FILOBLU is an App to deal with post-operation follow-up @ home



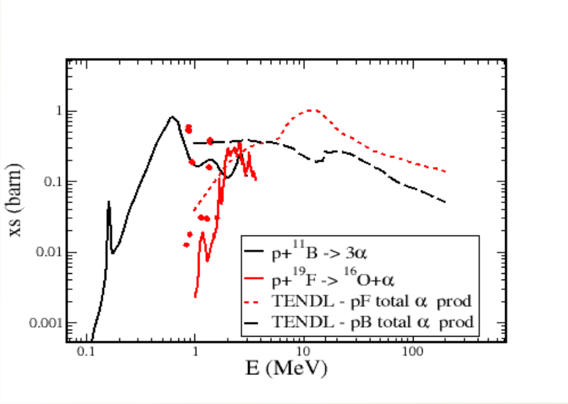
Evaluation of gravity of message (including sentiment analysis)

- Machine Learning is required to
  - Authomatic text analysis
  - Data Augmentation
  - Response classification

NEPTUNE
(19F-MRI)

→ Talk by Silvia Capuani

NEPTUNE
Nuclear process driven Enhancement of Proton Therapy UNravEled



Titolo	Nuclear process-driven Enhancement of Proton Therapy UNravEled
Area di ricerca	multidisciplinare
Responsabile nazionale	G Cuttone (INFN-LNS)
Unità partecipanti	LNS, Napoli, Roma1, Roma3, LNL, Milano, Pavia, TIFPA

PROJECT GOAL

Evaluate impact of ^{19}F and ^{11}B on particle therapy

GOALS OF WP2 (IMAGING)

RM1

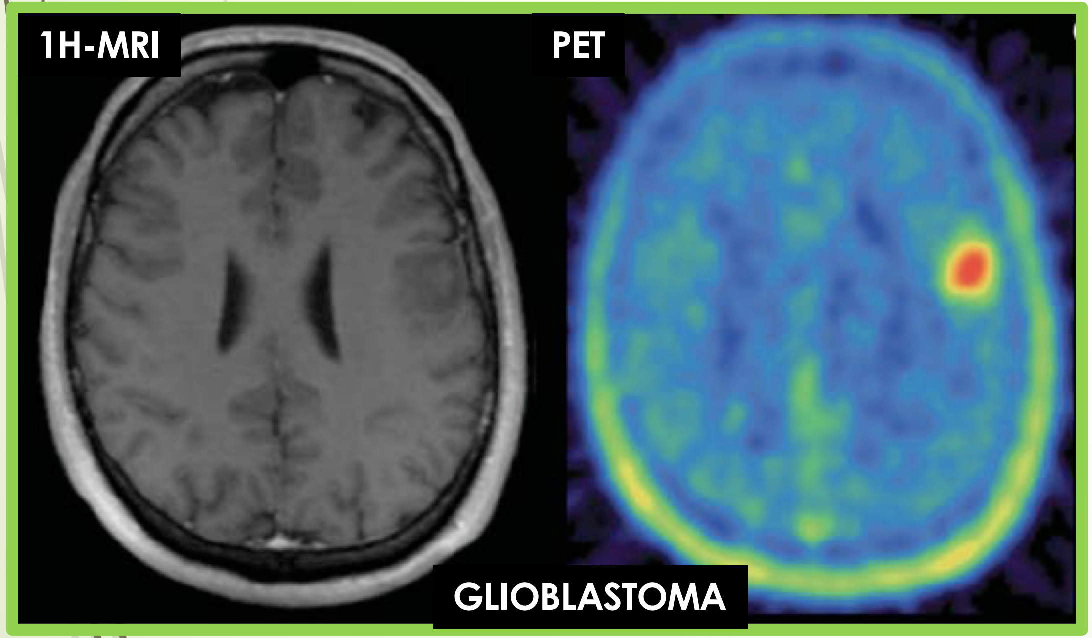
Evaluate bio-distribution of tracers

Evaluate concentration of samples

NA,PV

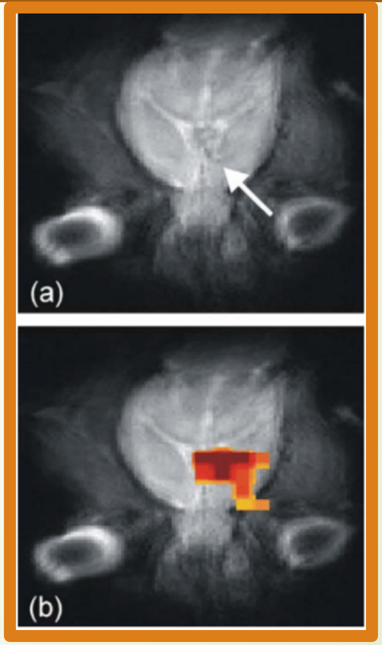
Available techniques: PET/MRI

PET has a worse resolution and tracers more difficult to synthetize/handle but 1H-MRI does not show a signal …



… but:

- gyromagnetic factor of 19F is only 6% away from 1H
- 19F is not present in human body (no physical background)



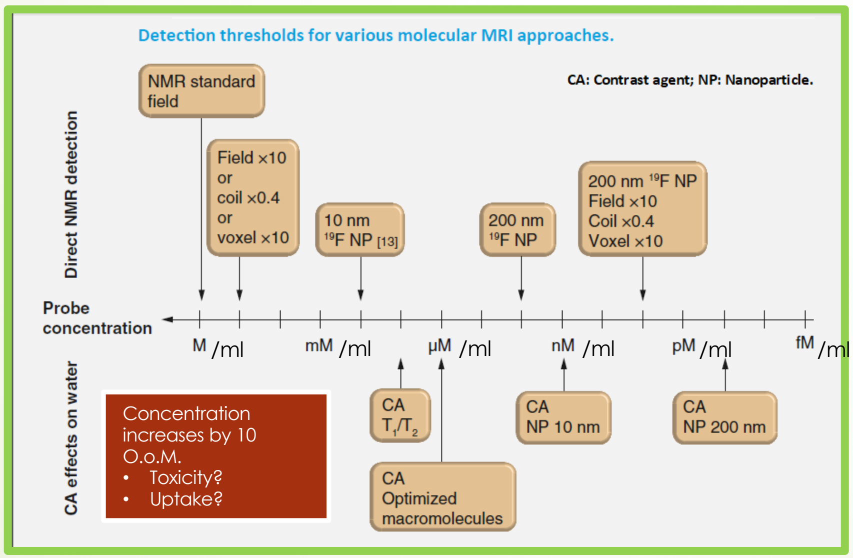
Concentrations and Performances

PET

- Typical PET activity concentrations:
  - Inject ~200MBq FDG (i.e. 3 10^{-12} moles), detect ~ 10^{-16} moles/ml

Cell Lines: PANCREAS(PANC-1)
Tracers: BSH
phenylalanine

MRI



Concentrations required by Particle Therapy:

- 80 ppm
- 0.11 mg/ml
- 10 μM/ml

Evaluation of bio-distributions of tracers

THIS PROJECT

A) Tests on animals to have samples with the correct concentration
B) Setup a test stand to study and improve, with INFN competences, the signal/noise ratio

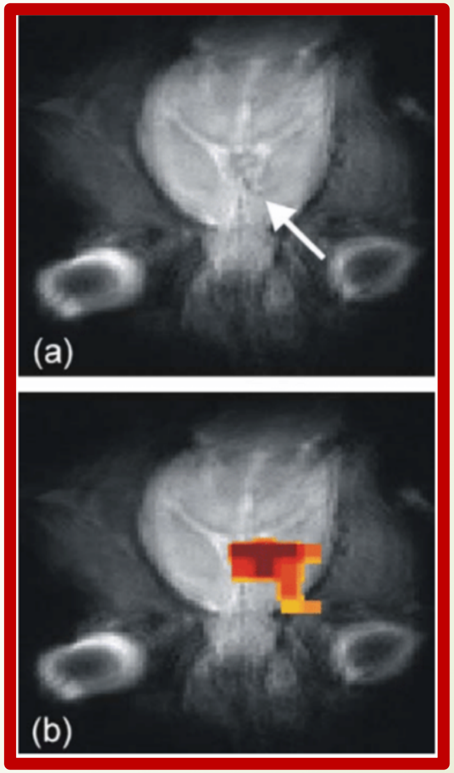
C) Study co-registered 19F and 1H images to study the noise correlation and possible algorithms to enhance sensitivity to signal

Study of co-registered 1H-19F analyses

Currently 1H and 19F images are only superimposed for visual comparison (combination is just product of signals)

Artificial Intelligence needed to:

- Align images
- Use autoencoders as de-noisers
- Segment 1H images
- Data augmentation



OUTLINE

NUCLEAR MEDICINE

CHIRONE
(Radio Guided Surgery)

HADRON THERAPY

FOOT
(RBE in PT)

FRED
(TPS with GPU)

DOSE PROFILER
(Particle Therapy dosimetry)

MONDO
(Fast Neutron Detection)

GENIALE
(Low Energy Nuclear Interactions)

ARTIFICIAL INTELLIGENCE IN MEDICINE → A. Retico

MARIANNE
(Imaging for stadiation)

→ Carlo Mancini Terracciano
e Cecilia Voena

NEPTUNE
(19F-MRI)

→ S. Capuani

FILOBLU
(Patient-Doctor interactions)

→ A. Ciardiello