



BNCT at University of Pavia

Saverio Altieri

Department of Physics University of Pavia, Italy

INFN Section of Pavia, Italy

5th NEU_BEAT Workshop
Rome - 2018 December 6h

Pavia University

Pavia is located in the North of Italy
about 30 Km south of Milan



The University of Pavia is one of the world's oldest academic institutions: it was founded in 1361 and until the 20th century it was the only university in the Milan area and the region of Lombardy.



Students are about 24,000
1500 from abroad

84 Undergraduate and Graduate programmes
17 Doctoral Programmes
42 Professional Master's Programmes



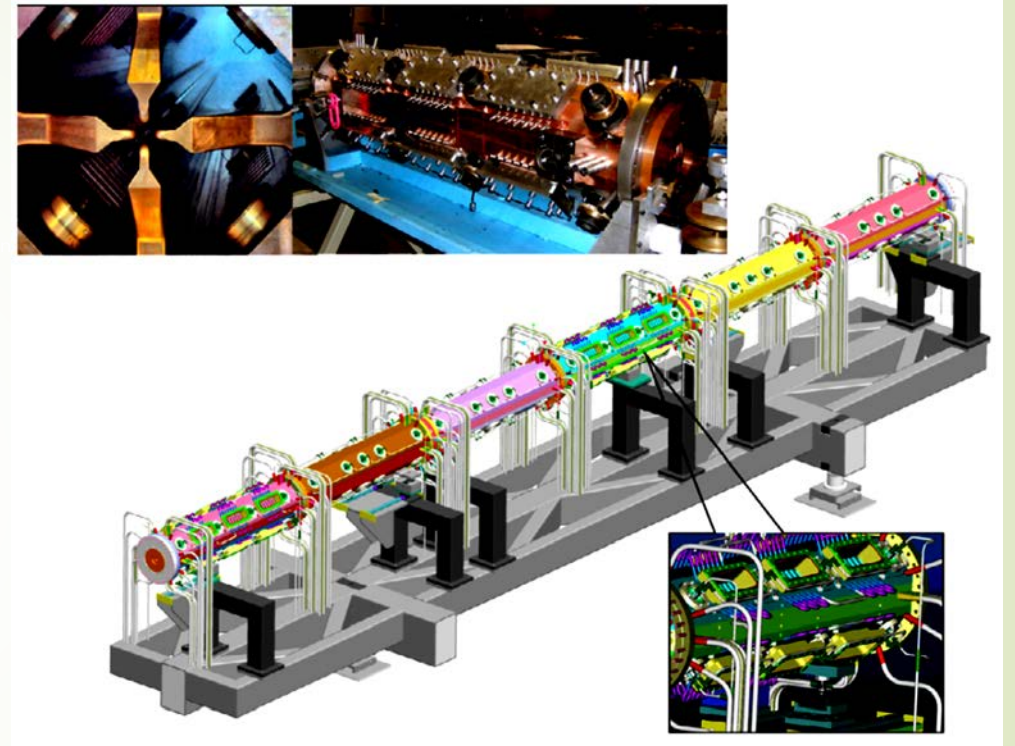
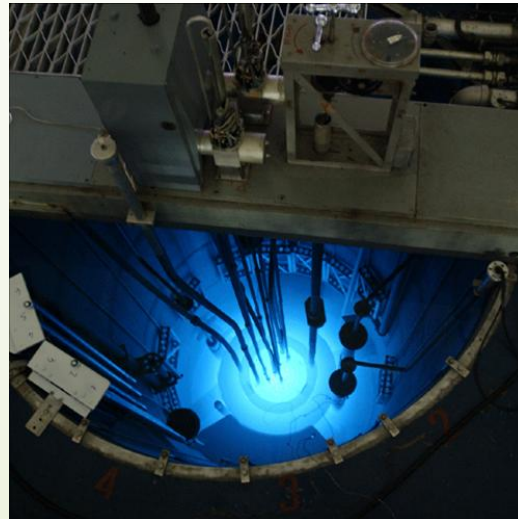
Applied Nuclear Energy Laboratory (LENA)



BNCT @ Pavia University and INFN

In Pavia we have a long tradition in BNCT research

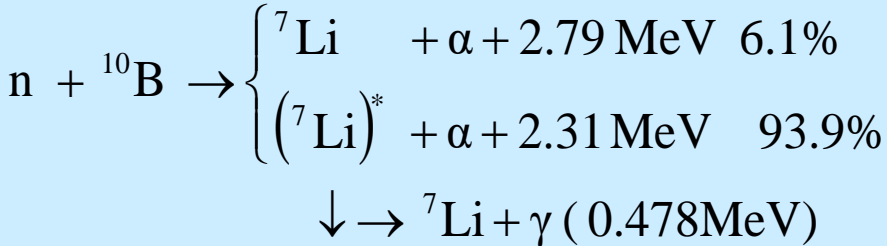
Our present neutron source is a 250 kW Triga Mark II research reactor



Channel D

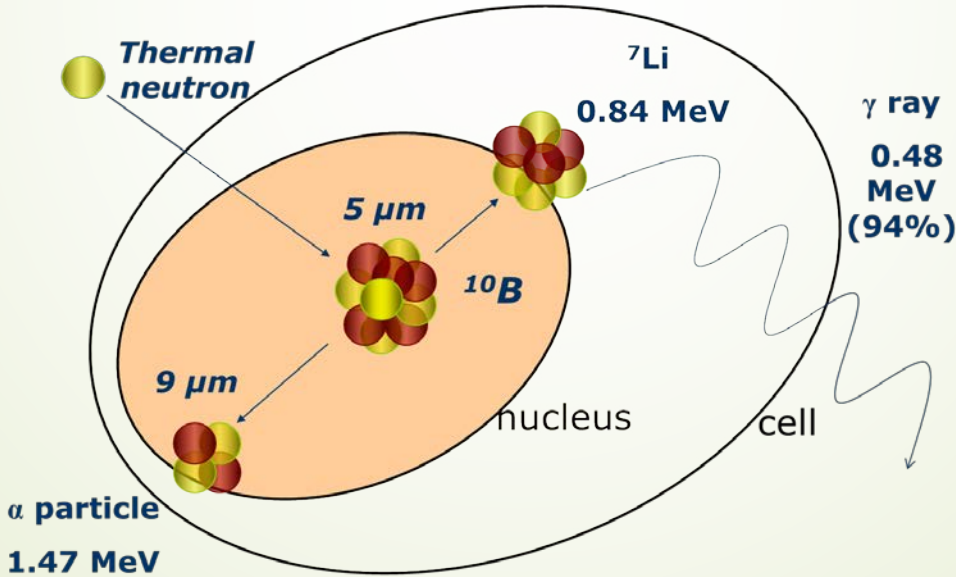
We are planning to install an
accelerator based
BNCT facility
at National Hadron Therapy
Center (CNAO) in Pavia

BNCT principle

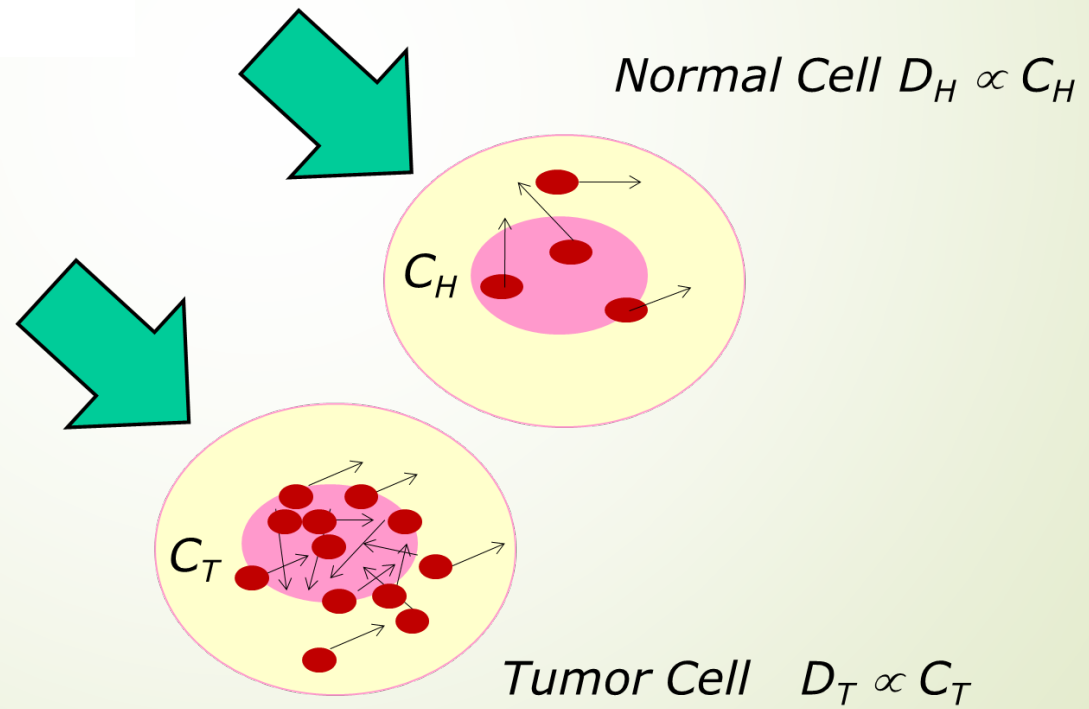
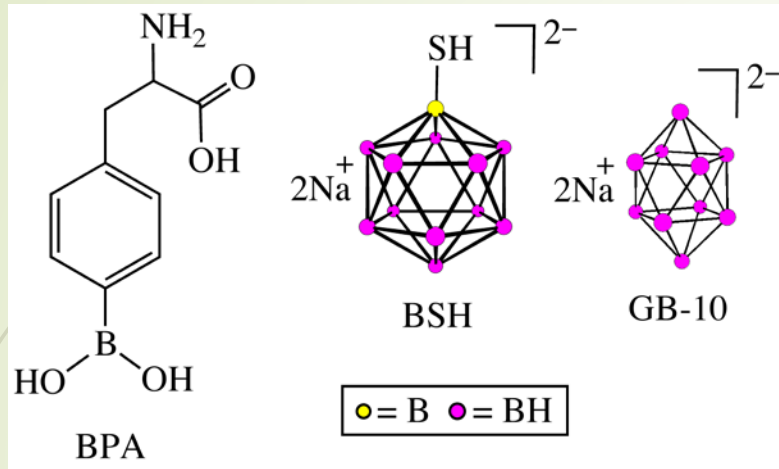


$$R_\alpha \cong 8 \mu\text{m}$$

$$R_{\text{Li}} \cong 5 \mu\text{m}$$



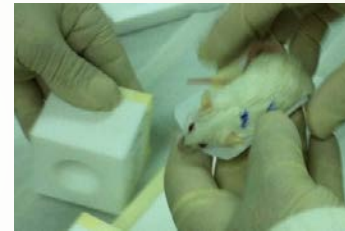
BNCT selectivity



BNCT @ TRIGA Mark II reactor



- Disseminated liver metastases: **TAOrMINA project**
- Test of toxicity and effectiveness of BNCT by irradiating cell cultures and animal models of rats and mice treated with new boron compounds
 - Disseminated lung metastases
 - Mesothelioma
 - Limb osteosarcoma
- Research of new boron carriers: boron up-take measurements in vitro and vivo in animal models
- In vivo boron dose imaging system based on Zinc Cadmium Telluride
- Give our support to create an accelerator based BNCT center at CNAO



Extra-corporeal liver BNCT for diffused metastases

After BPA infusion the liver was

exsplanted



washed and refrigerated



placed in a teflon container



irradiated in the thermal column

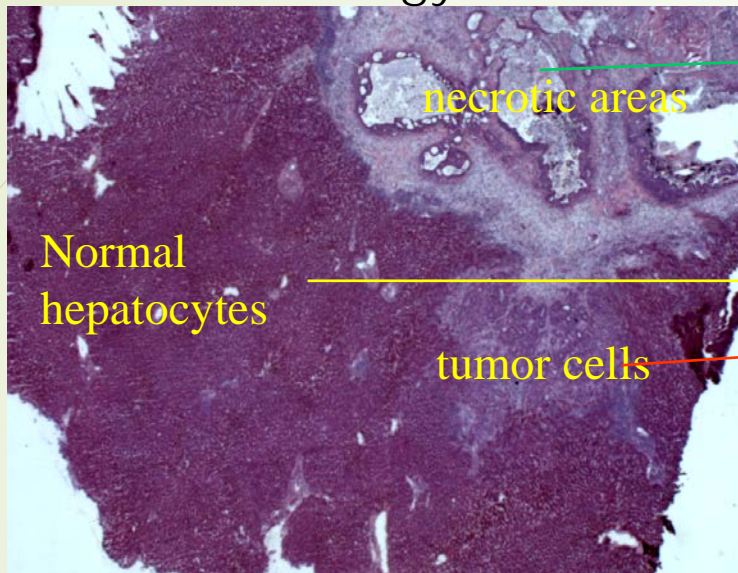


sent back to the surgery room

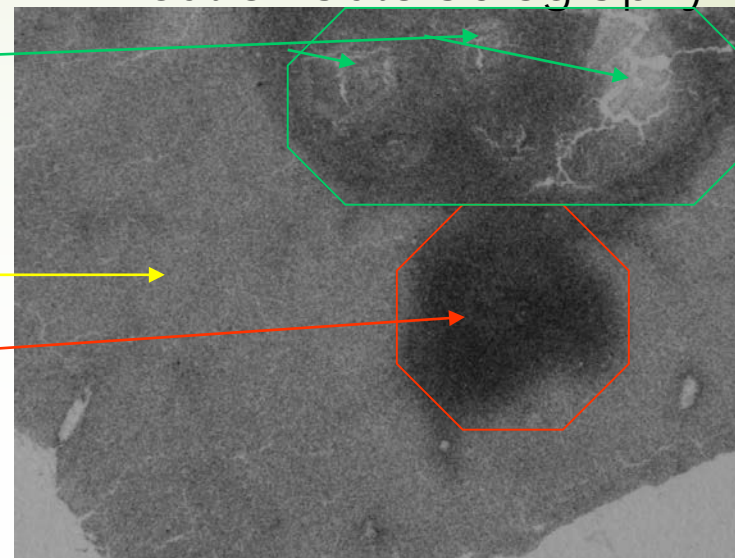


Selective Boron up-take in metastases

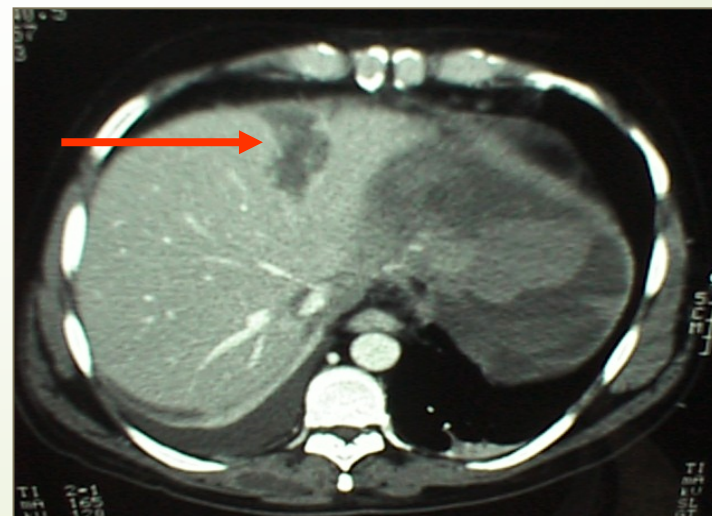
histology



neutron autoradiography



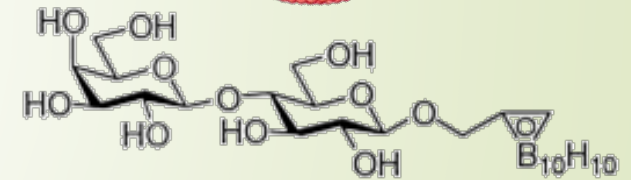
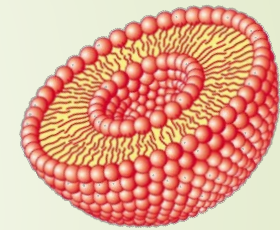
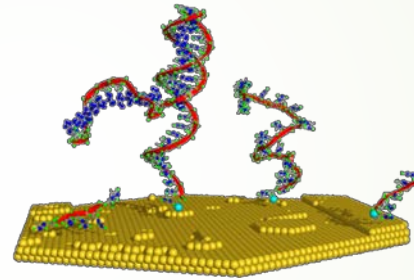
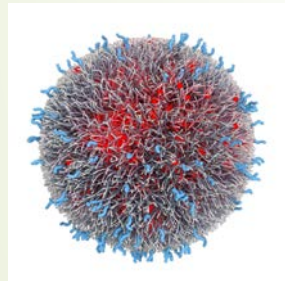
Selective metastases destruction



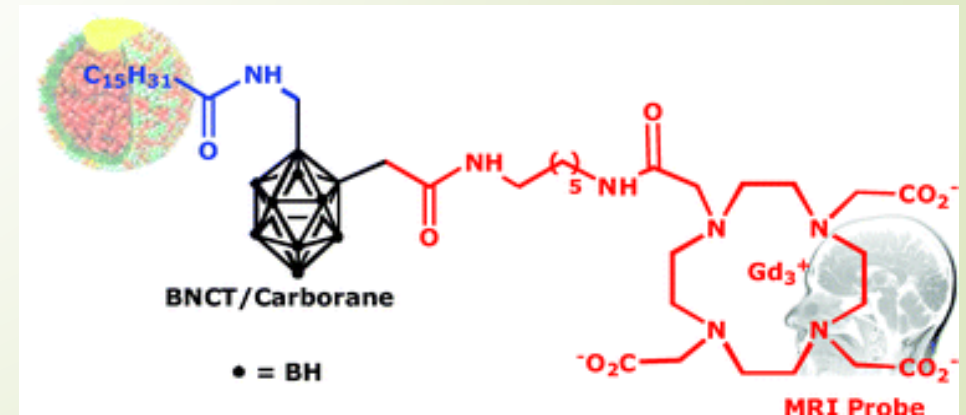
New borated formulation tests in vitro and in vivo

After Taormina project we started studying the possibility to apply BNCT without autotransplantation but using external beam and new boron carriers for the treatment of

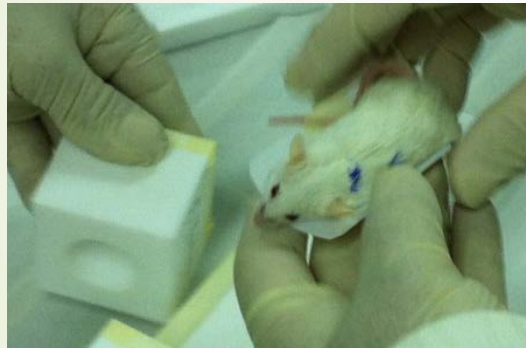
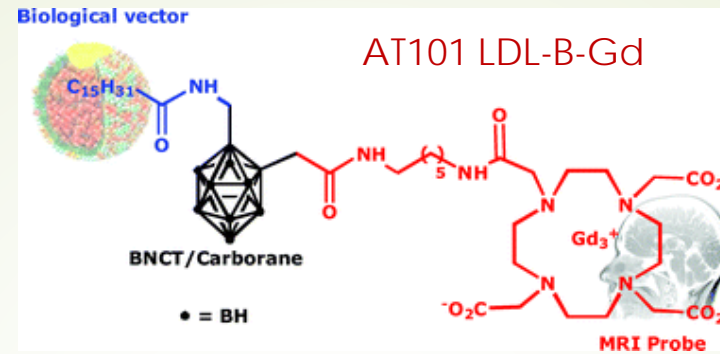
- Disseminated lung metastases
- Mesothelioma
- Limb osteosarcoma



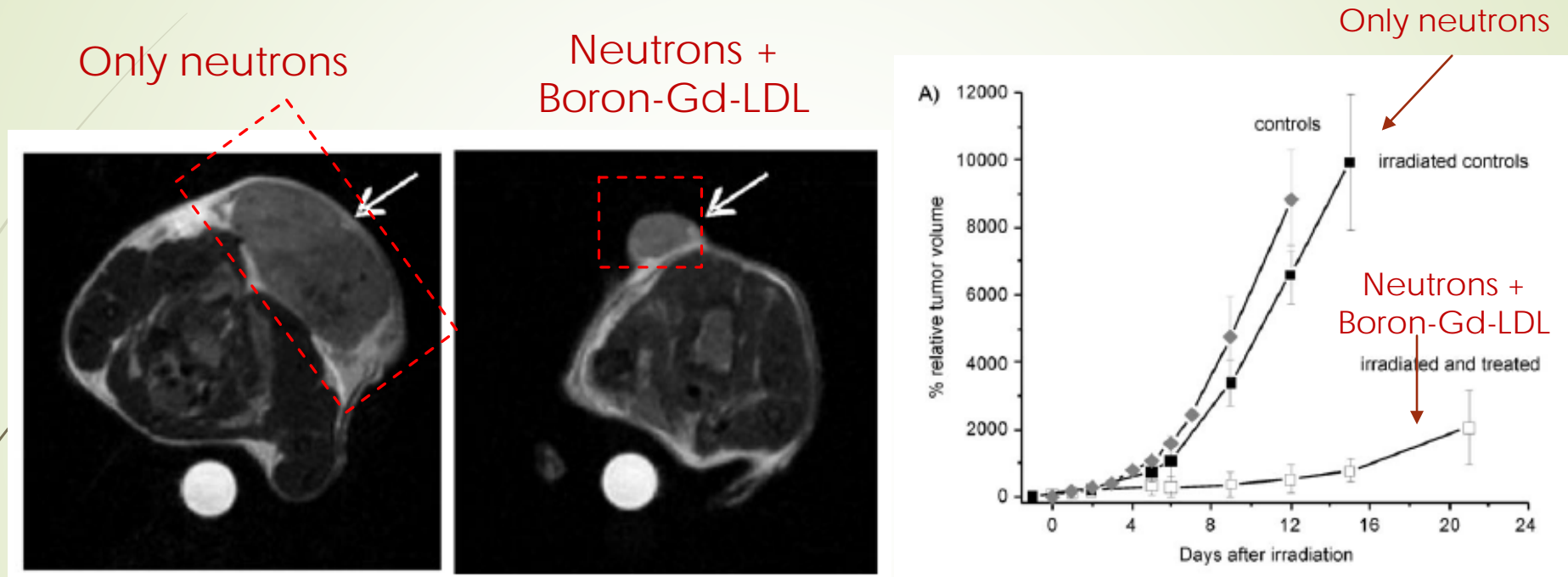
- In vitro test of uptake
- In vitro test of effectiveness (survival curves)
- In vivo test of selectivity (imaging and quantitative measurements)
- In vivo test of effectiveness (small animal irradiation)



LDL-Boron-Gd adduct: BNCT effectiveness in mice

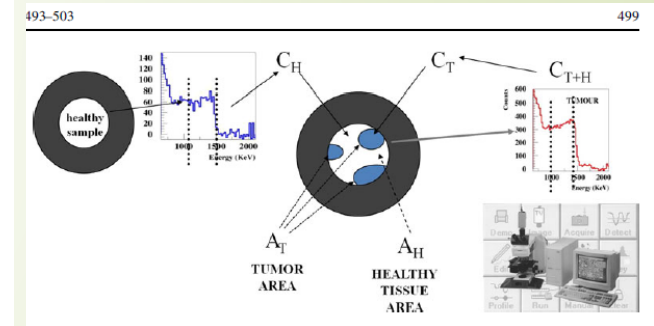
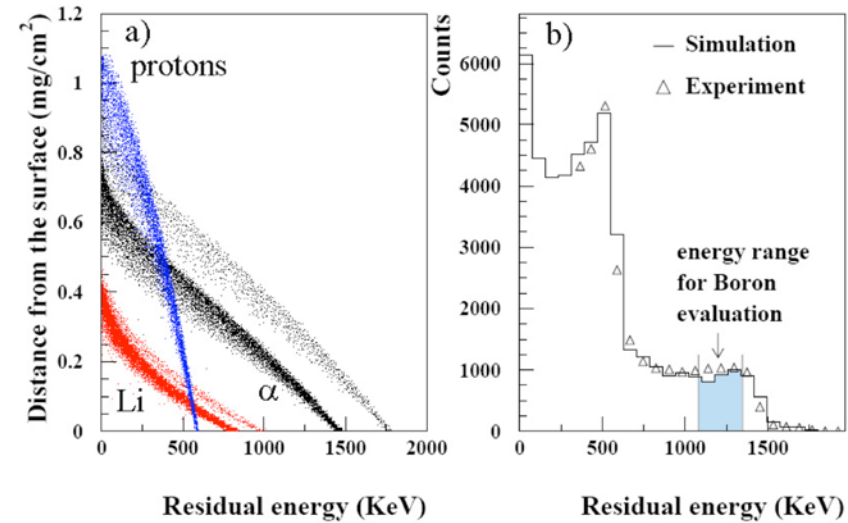
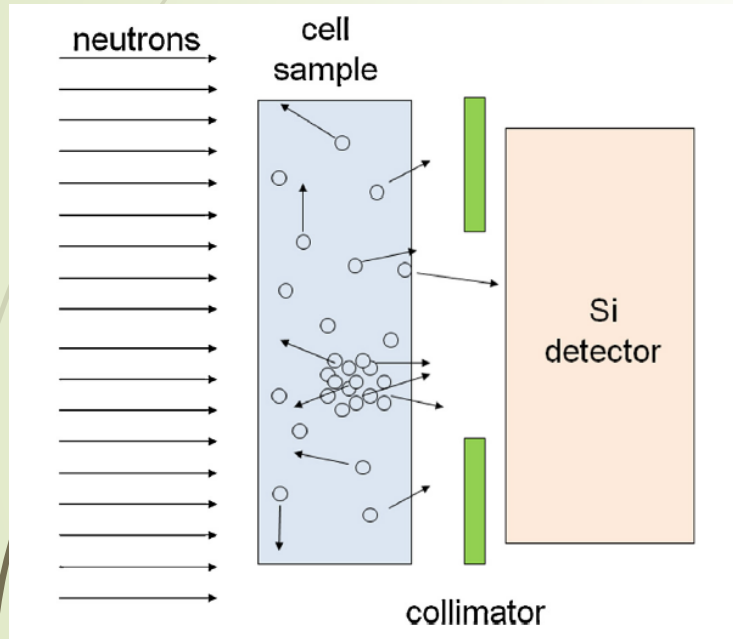
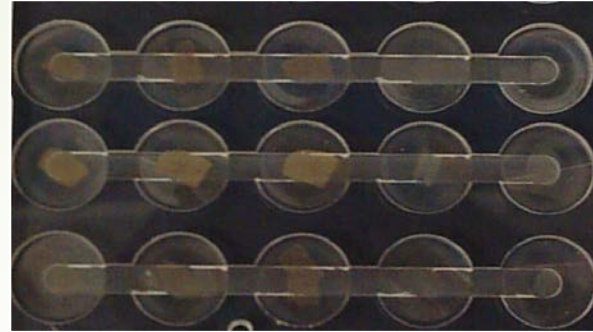
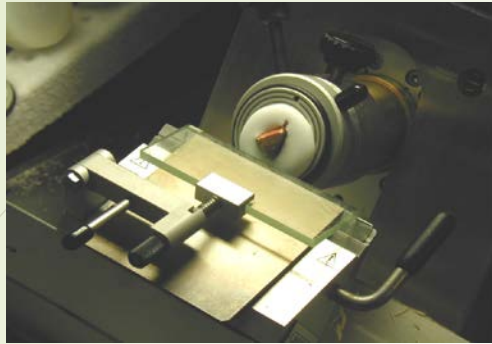


Boron-Gd-LDL: B16F10 melanoma bearing C57BL/6 mice

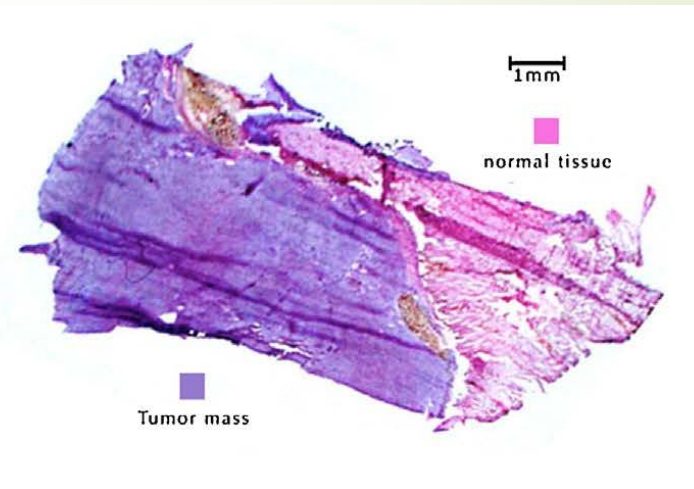
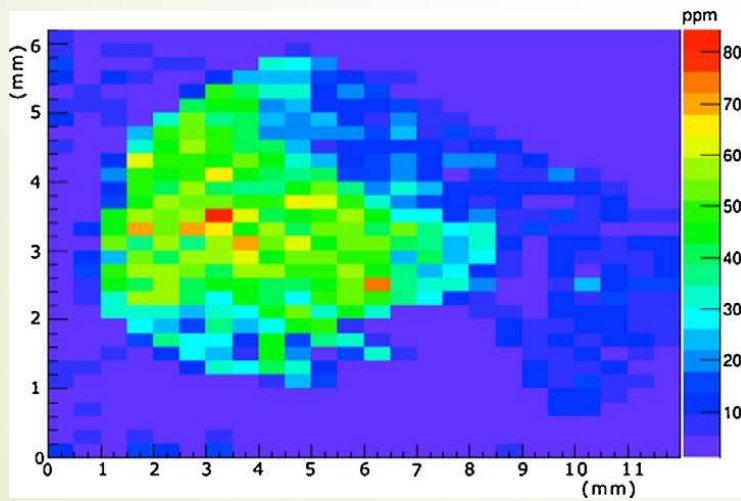
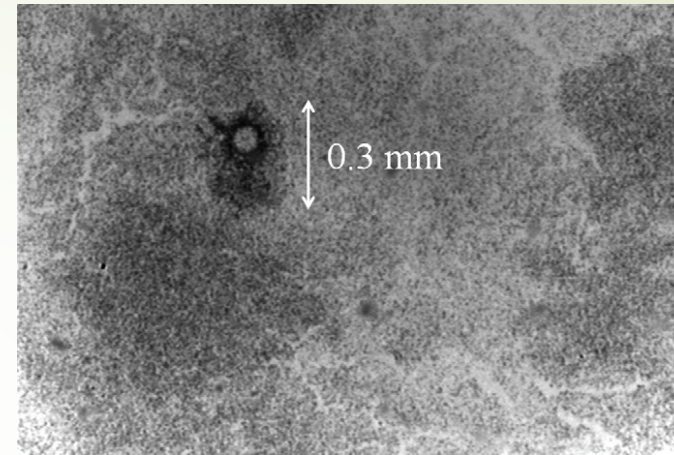
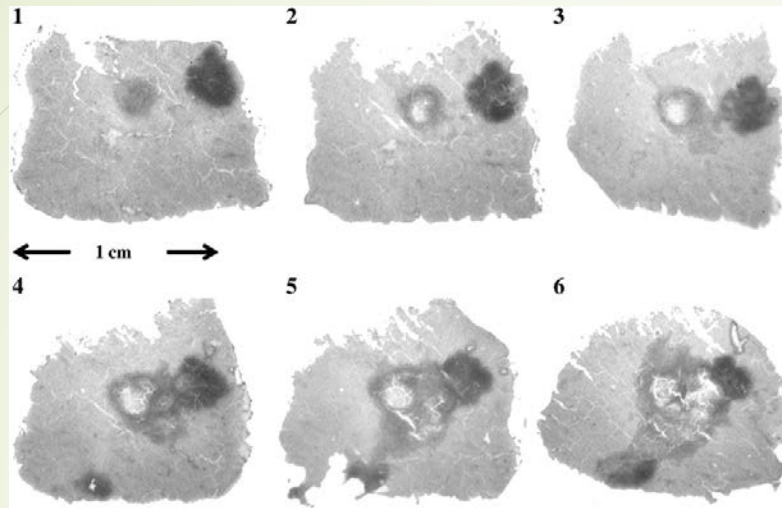


The tumour growth was followed by MRI for 20 days after irradiation

Boron concentration measurement by a spectrometry



Boron concentration measurement by neutron autoradiography



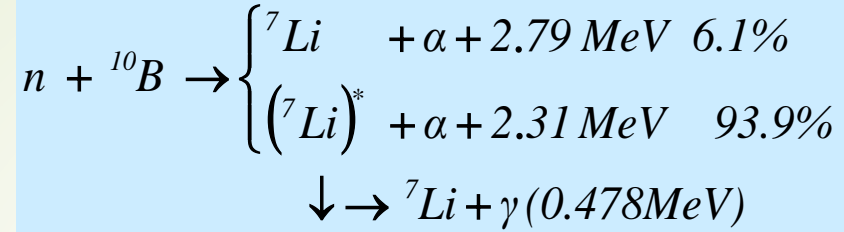
Online Boron dose imaging by SPECT with CdZnTe detector

in collaboration with

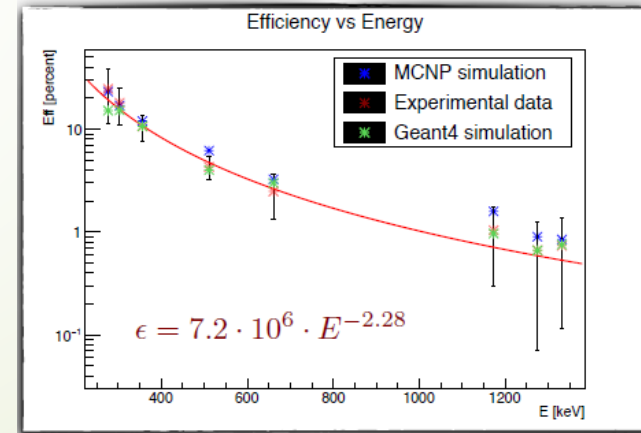
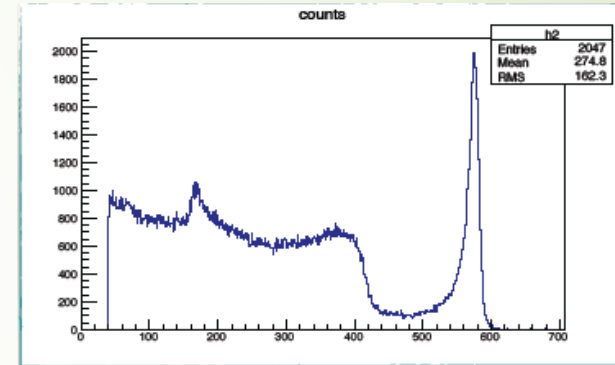
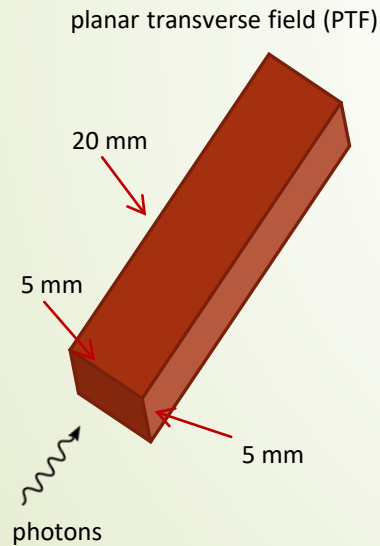
**Institute of Materials
for Electronics and
Magnetism**

Italian National Research Council

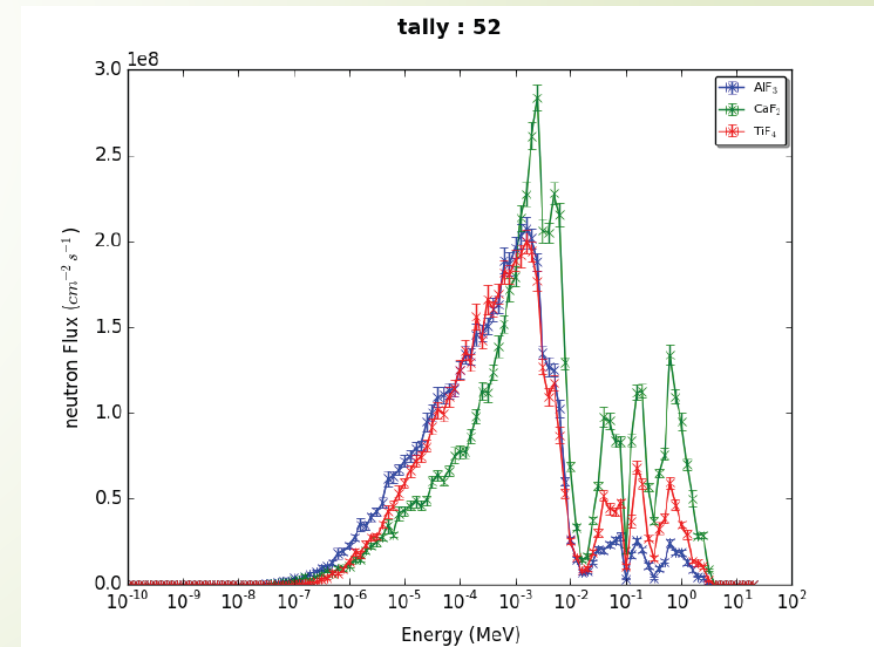
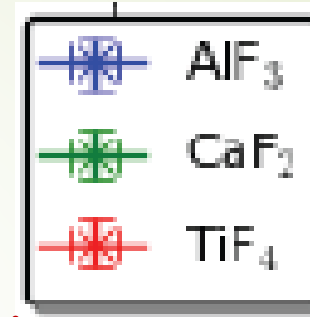
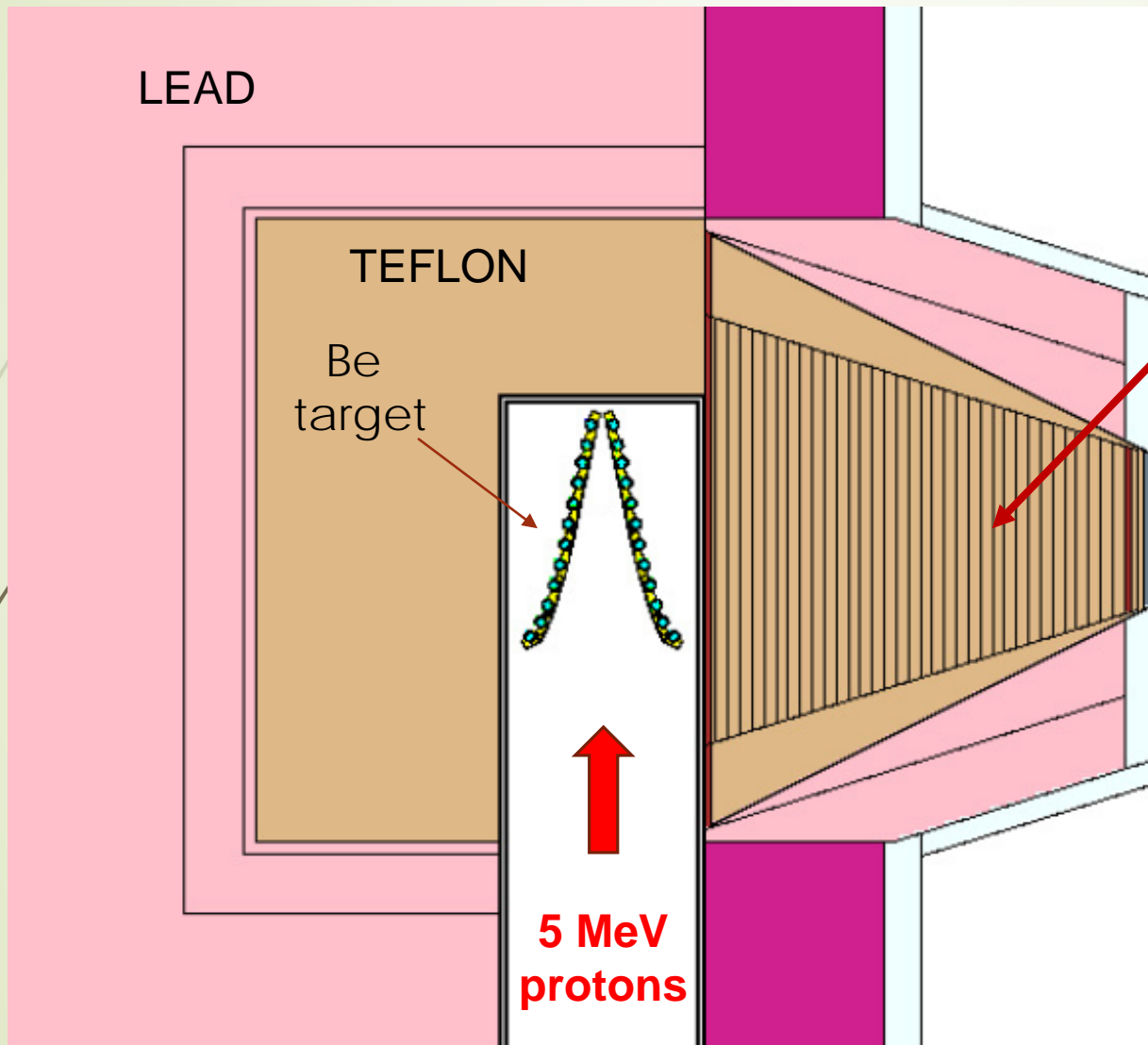
IMEM-CNR
Parma



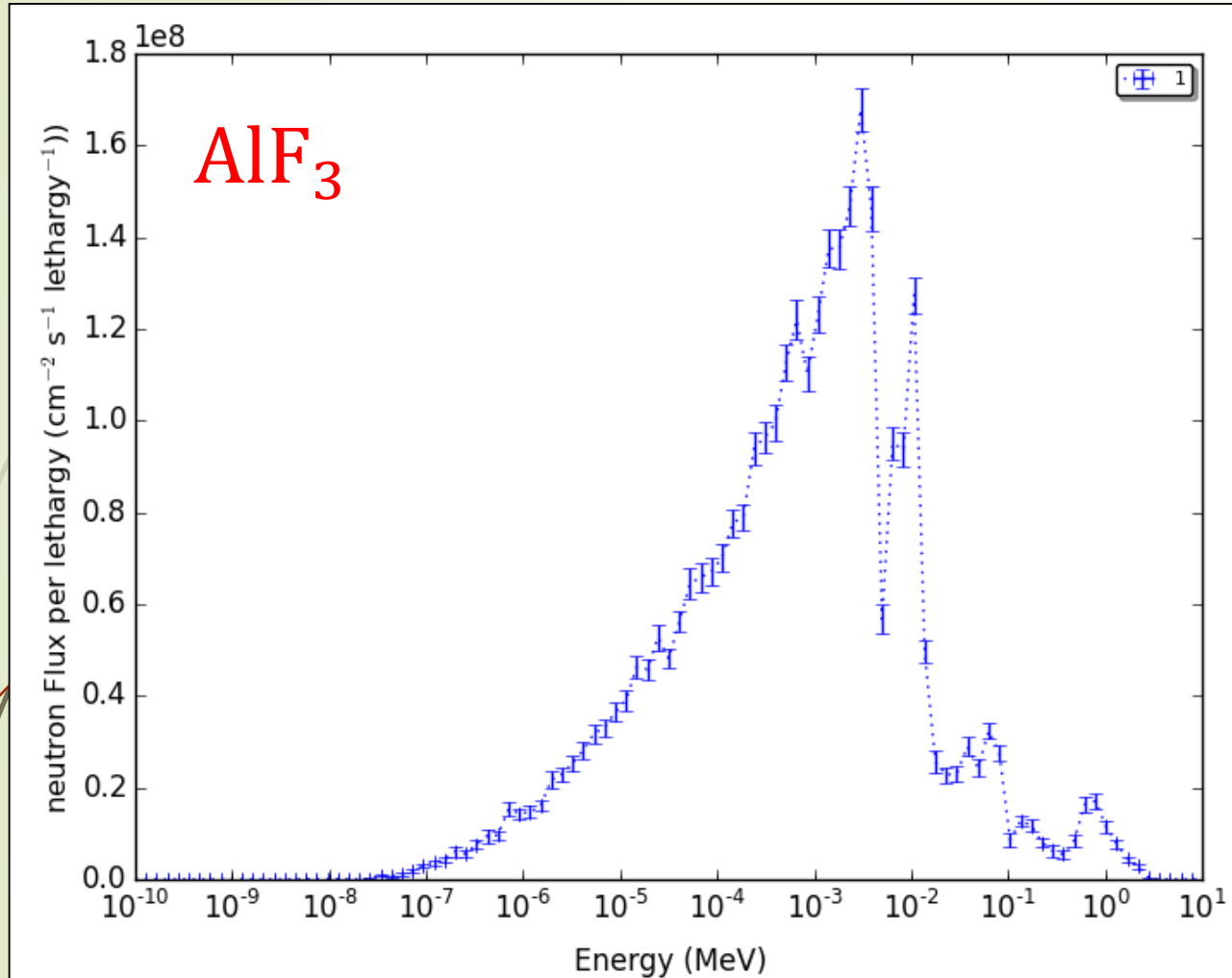
1D detector under test: a drift strip detector $0.5 \times 0.5 \times 20 \text{ mm}^3$



Beam Shaping Assembly Monte Carlo studies



Tailoring of a neutron beam around 1 keV

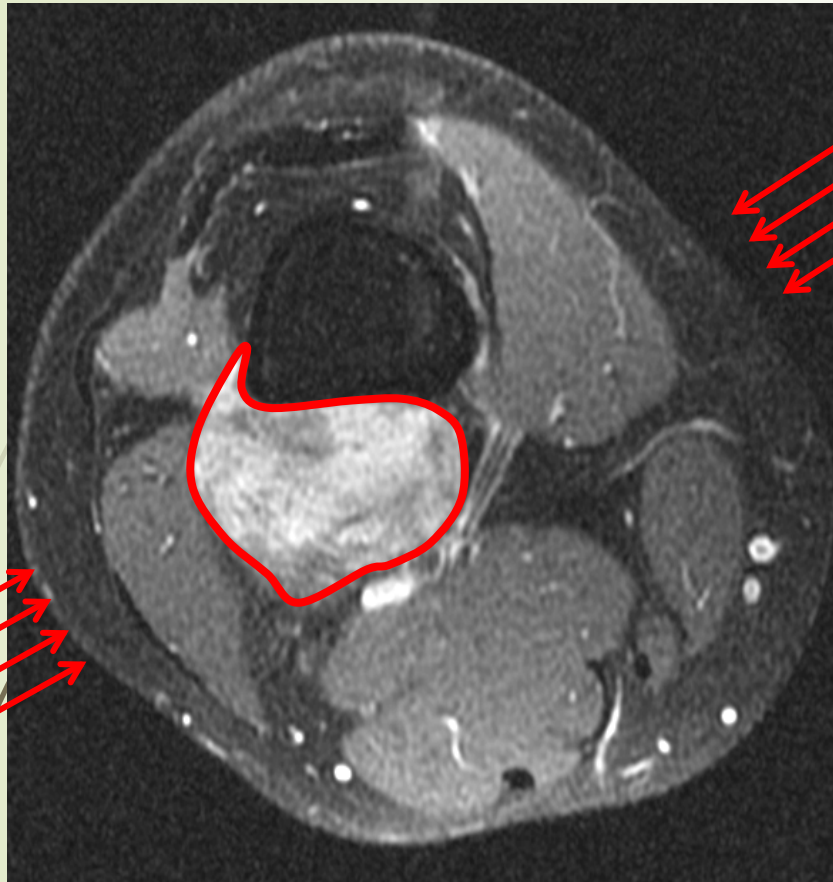


FIGURES OF MERIT

Flux	$2.8 \cdot 10^9 \text{ cm}^{-2} \text{ s}^{-1}$
Fast cont	$8.9 \cdot 10^{-13} \text{ Gy cm}^2$
Gamma cont	$3.7 \cdot 10^{-13} \text{ Gy cm}^2$

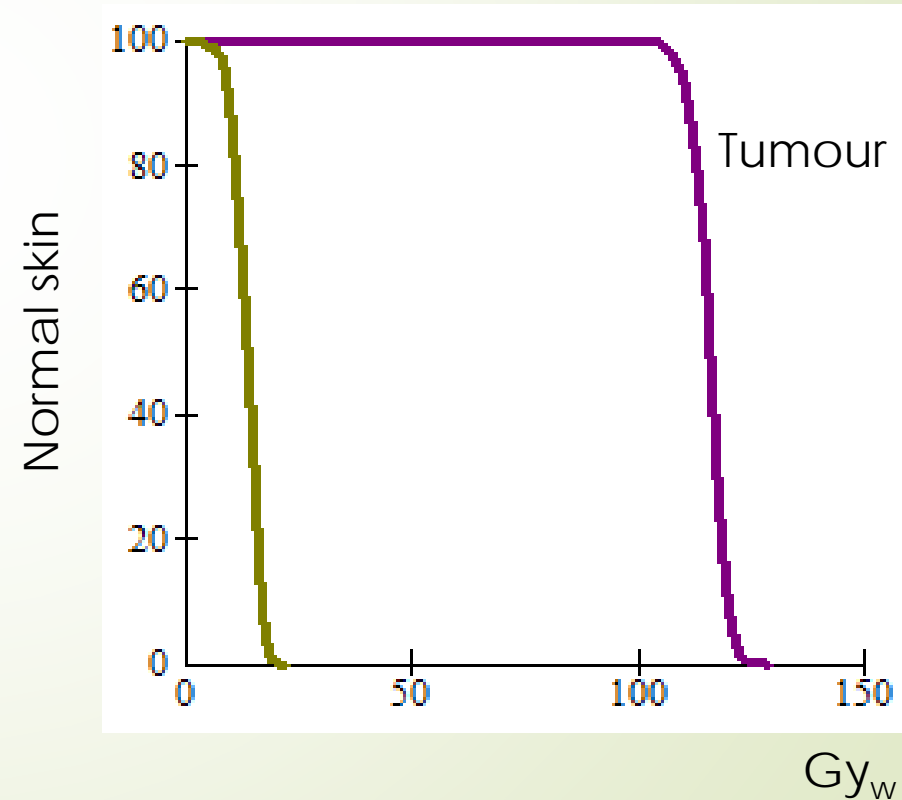
p+

Validation of the beam with a TPS



Limb Osteosarcoma

The prescription of 22 GyEq to skin, leads to a tumour dose of 99.3 – 129 Gy_Eq with a good uniformity in all the tumour volume



Sintering of AlF_3

Design and construction and characterization of a prototype of syntherization machine @INFN workshop **in collabroration with Chemistry Department** of Pavia

Powder

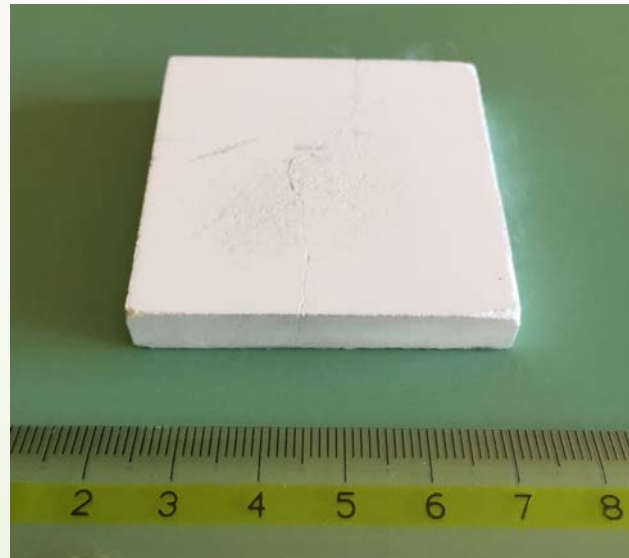


Pressure + temperature

Solid AlF_3



density 99%

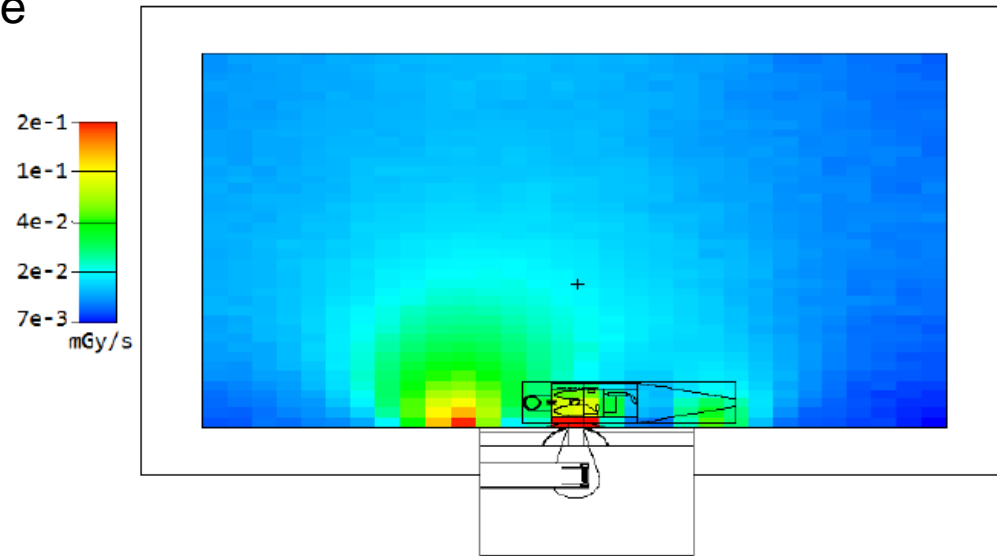


50x50x10 mm density 82%



BNCT treatment room and patient activation studies

Absorbed dose MESH in the room with walls of ordinary concrete



	Dose in 2h [mGy]	
	ordinary concrete	concrete+boron
brain	773±7	573±5
bladder	415±11	329±7
stomach	419±7	363±5
kidneys	526±7	450±6
intestine	624±7	548±5
lungs	501±4	490±3
liver	122±11	115±7

Table 4.3: Doses absorbed by the principal organs in 2h of irradiation

Nuclide	Half-life [s]	R [s ⁻¹ g ⁻¹]	a [Bq/g]
Cl-38	37.24 min	34.98 ± 0.07	23.53 ± 0.04
K-42	12.360 h	30.80 ± 0.06	1.680 ± 0.003
Fe-59	44.503 d	0.4180 ± 0.0011	0.0002712 ± 0.000007

Table 5.3: Simulated reaction rates and specific activity after 2h of irradiation for soft tissue elements, with the walls of ordinary concrete

Italian collaboration

University of PAVIA

Department of Physics

Department of Clinical-Surgical, Diagnostic and Pediatric Sciences

Department of Chemistry, University of Pavia

Department of Molecular Medicine, University of Pavia

INFN, Pavia

INFN - LNL, Legnaro

CNAO, Pavia

University of TORINO

University of NOVARA

University of Palermo

IMEM-CNR Parma

Due2lab s.r.l. Parma

INAF-OAS, Bologna

International collaborations

❑ *China* Funded project in the frame of the Executive Programme of Scientific and Technological Cooperation between Italy and China for the years 2016-2018. Italian Ministry of Foreign Affairs and International Cooperation (MAECI). Project: NEU_BEAT (Neutron Beams for Cancer Treatment). Collaboration on:

- New materials for neutron beams design
- Treatment Planning calculations
- Computational dosimetry
- Integration of BNCT and heavy ion therapy

❑ *CNEA, Argentina: very active researchers exchange for computational dosimetry, treatment planning, beam design, B concentration measurement methods inter-comparison, BNCT efficacy and toxicity on animal models,*

- ❑ *INL, Idaho, USA: neutron spectrometry in irradiation facilities*
- ❑ *HUCH, Helsinki University Central Hospital and FIR 1, Finland*
- ❑ *QEH, University Hospital, Birmingham*
- ❑ *Okayama University*
- ❑ *Nagoya University*



Thank you

saverio.altieri@unipv.it

<http://www.bnct.it>