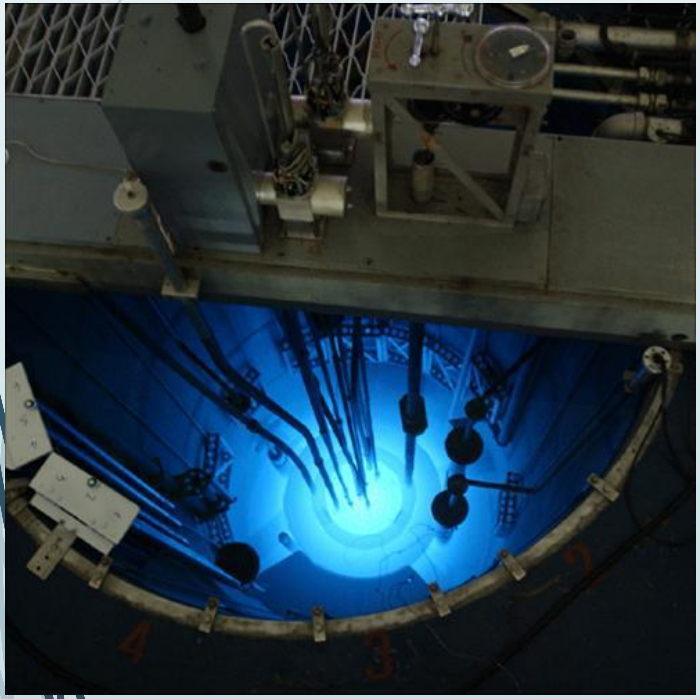
JORNADAS DEL CUIA EN ARGENTINA 10a. Edición

Pavia reactor based neutron source and liver treatment



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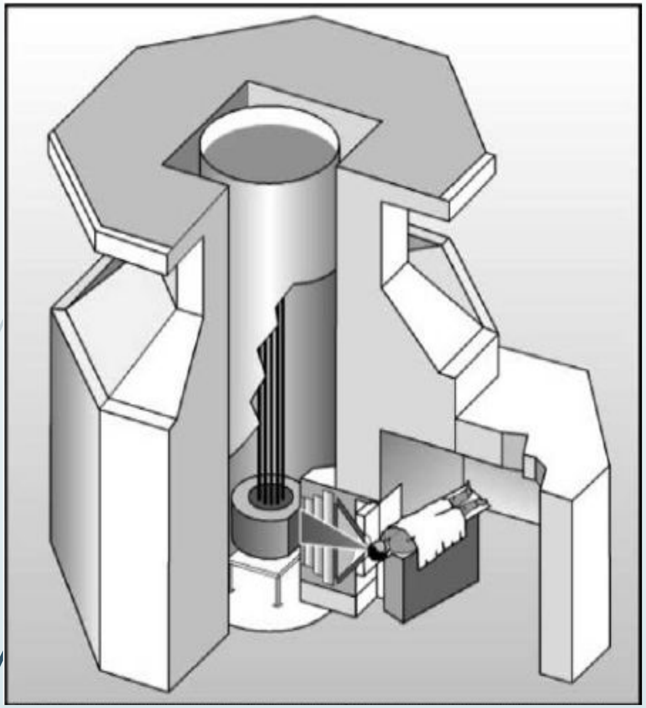
and
National Institute for Nuclear Physics
(INFN) Section of Pavia, Italy

Neutron sources for BNCT

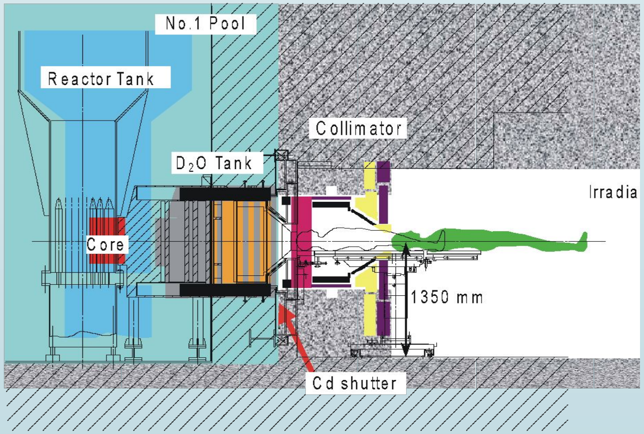
$$\varphi_{th} = 10^9 cm^{-2} s^{-1}$$

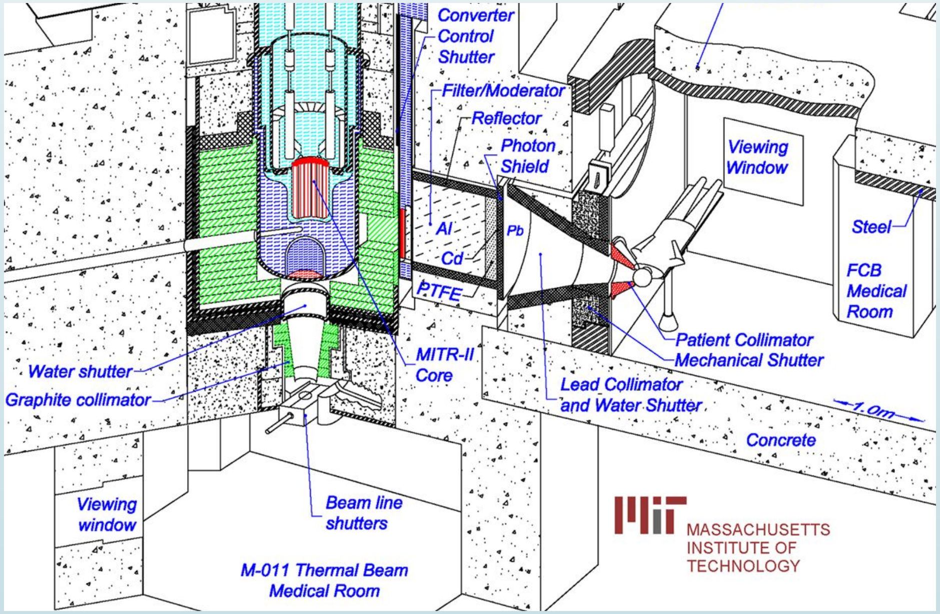
in the tumour



Nuclear Reactors

until now



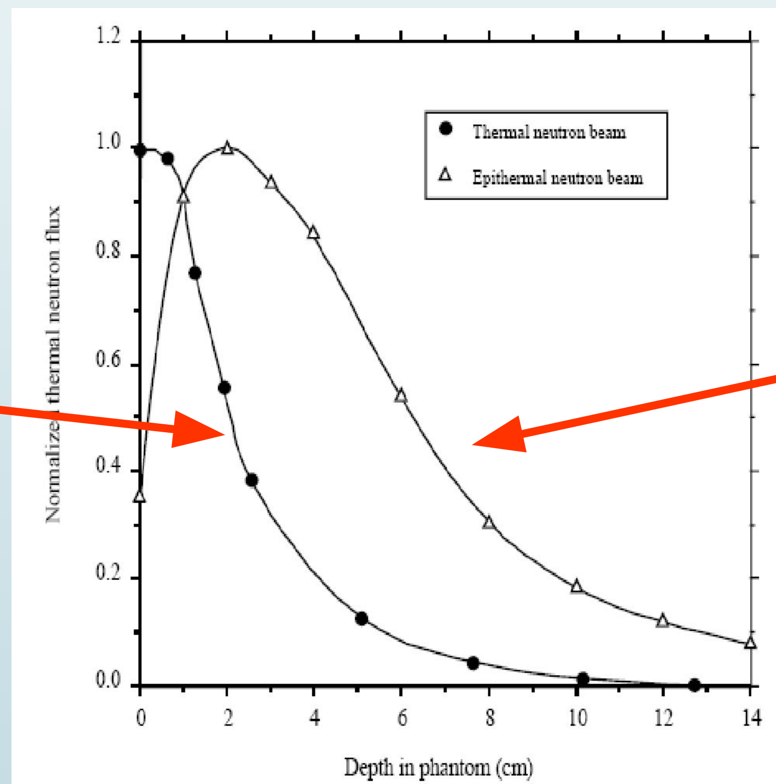


Neutron energy for BNCT: thermal neutrons profile

Neutrons Beam

thermal or epithermal

thermal neutrons profile in the phantom

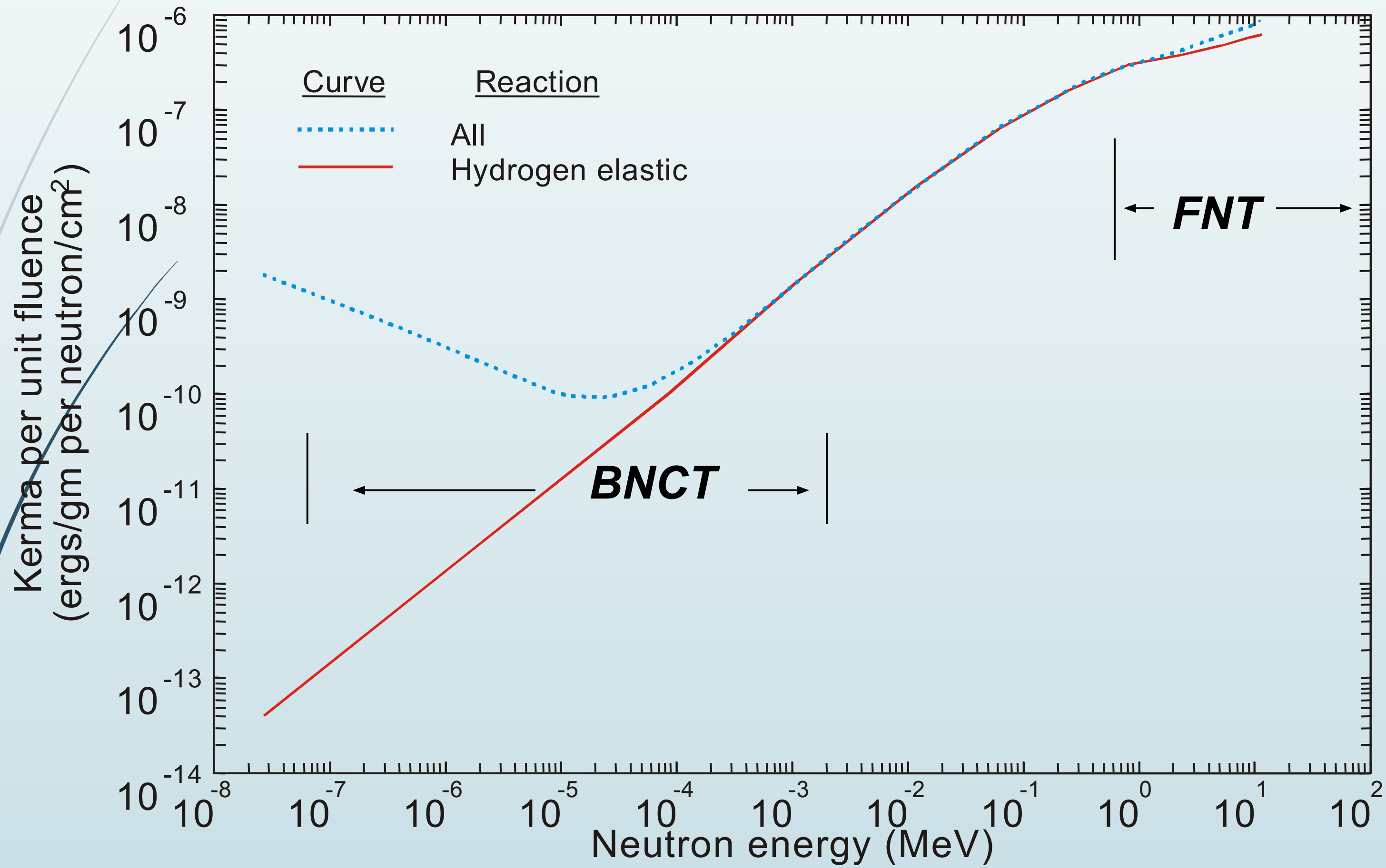


Starting with thermal neutrons

Starting with epithermal neutrons

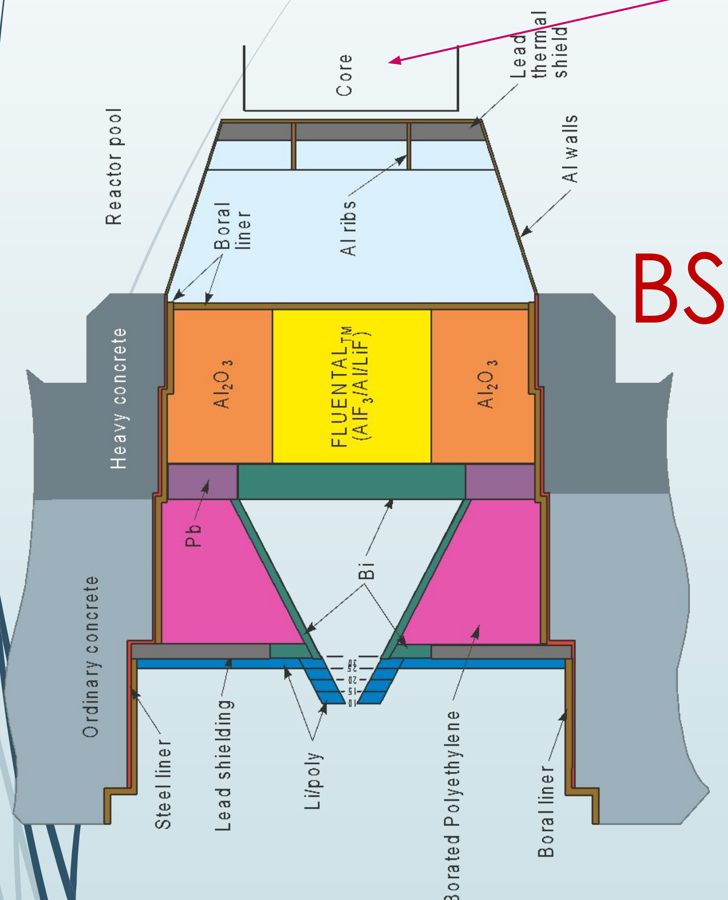
Neutron sources for BNCT: energy range

Neutron kerma in healthy tissue



Neutron sources for BNCT: Beam Shaping Assembly

reactor core

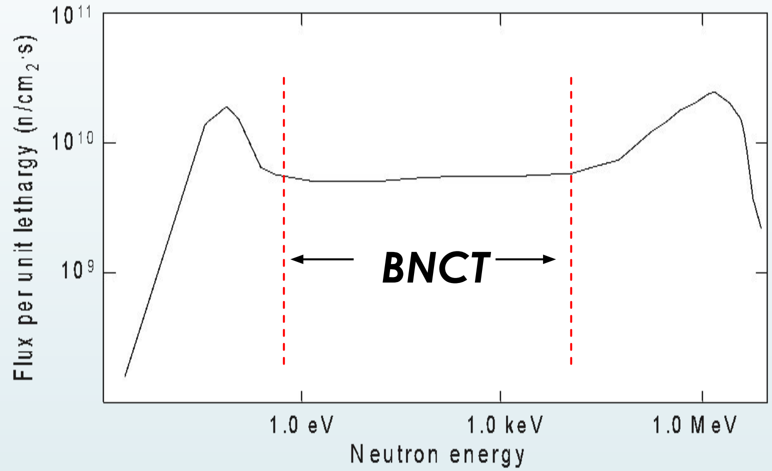


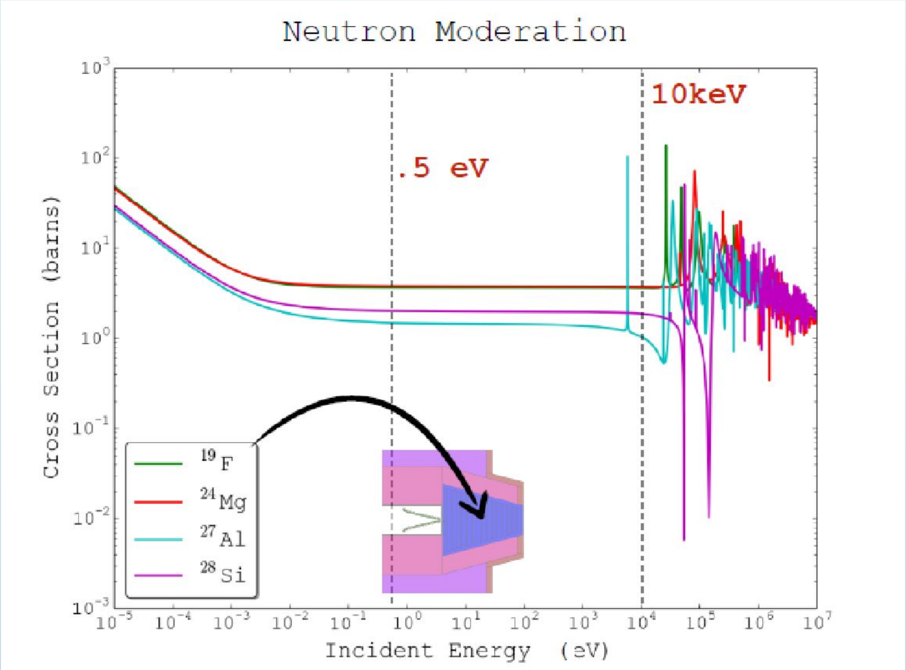
BSA

patient position

WSU Epithermal Filter

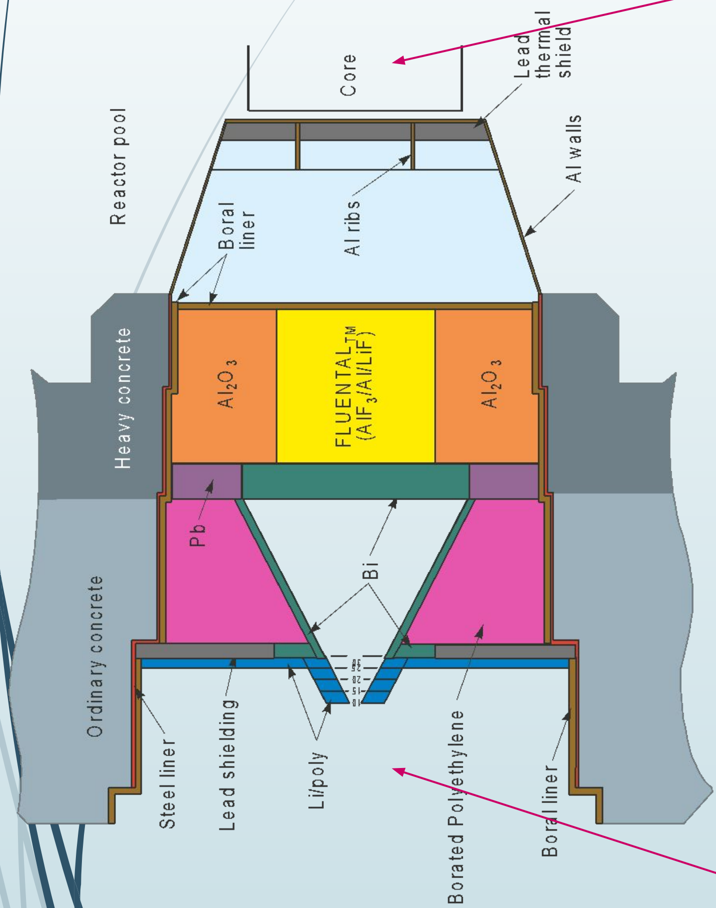
Typical Unfiltered Neutron Spectrum





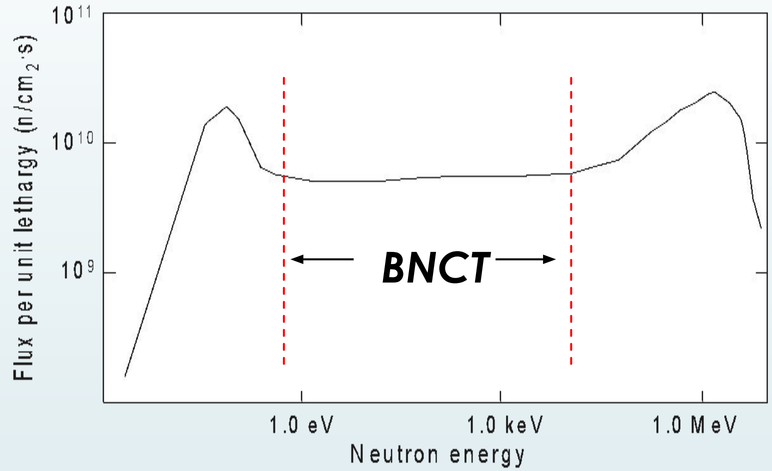
Neutron sources for BNCT: Beam Shaping Assembly

BSA

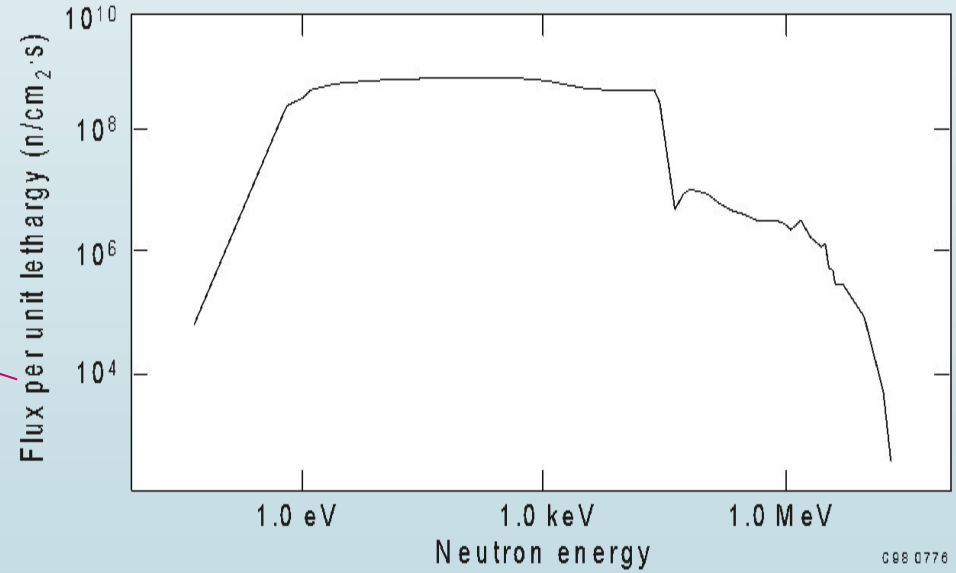


WSU Epithermal Filter

Typical Unfiltered Neutron Spectrum

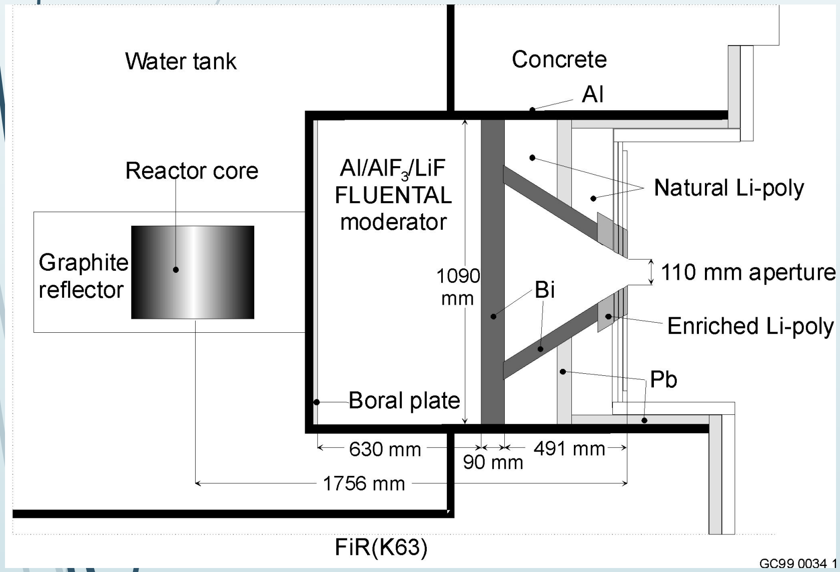


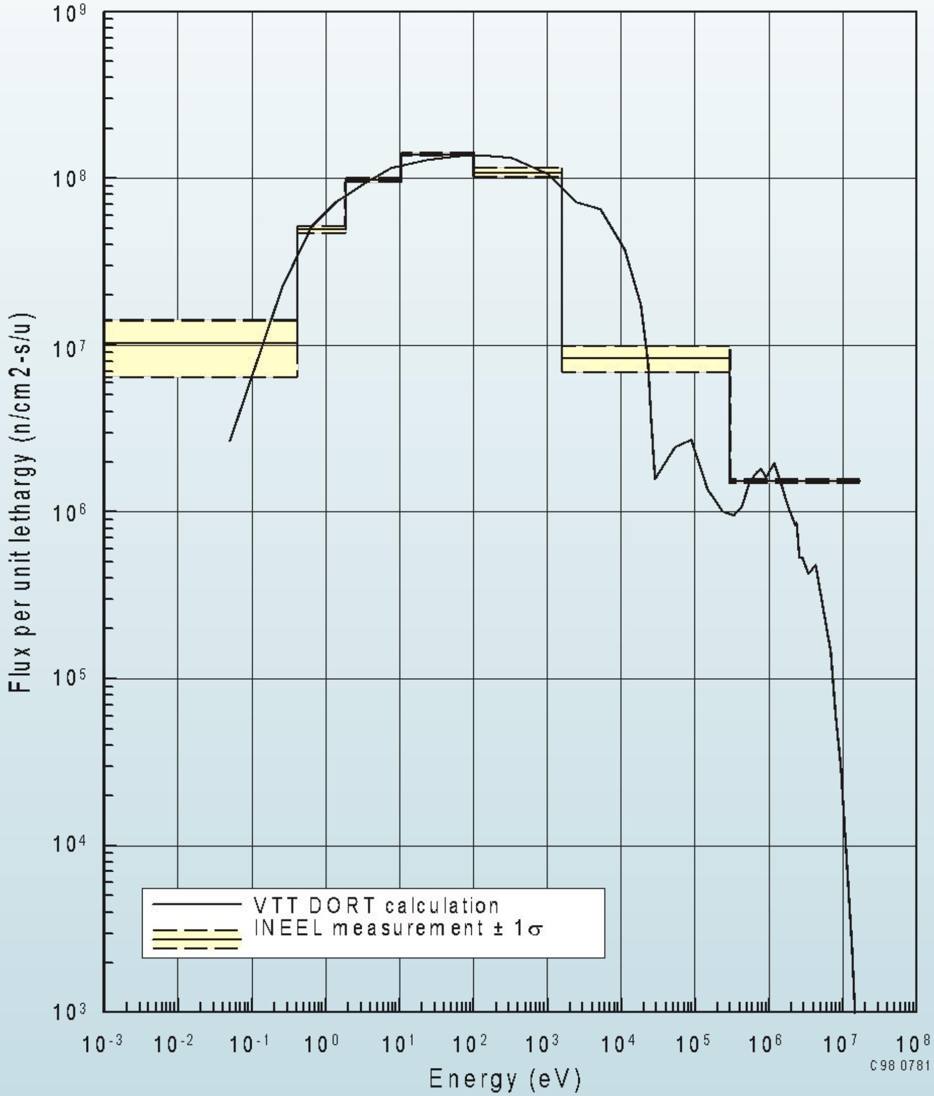
Epithermal-Neutron Spectrum for BNCT



Neutron sources for BNCT: Beam Shaping Assembly

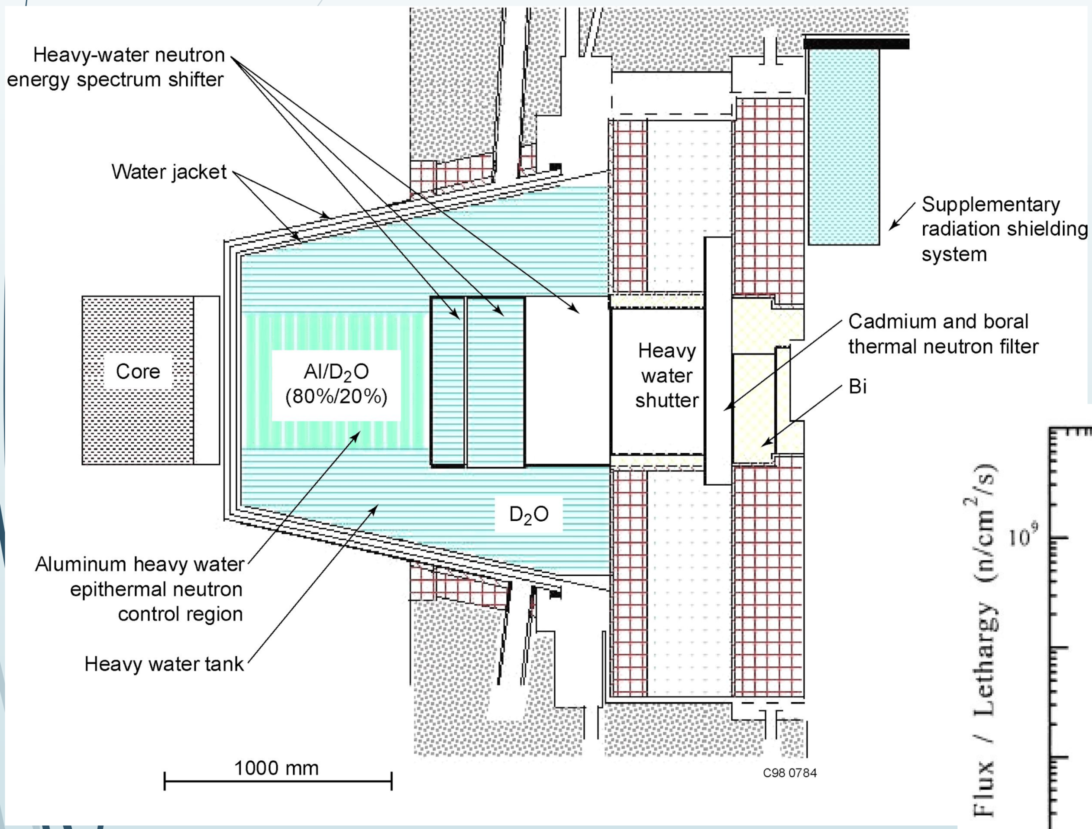
FiR-1 Finland

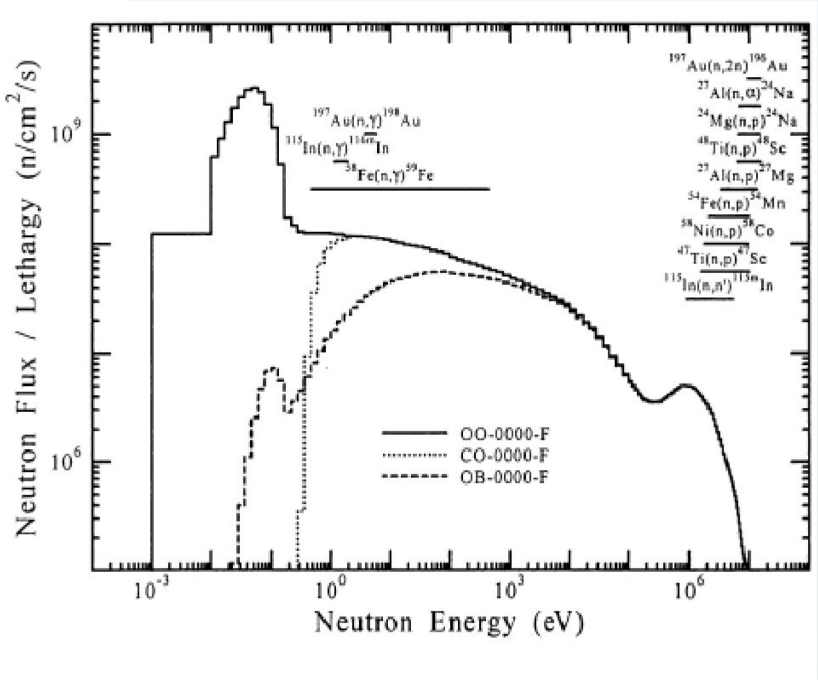




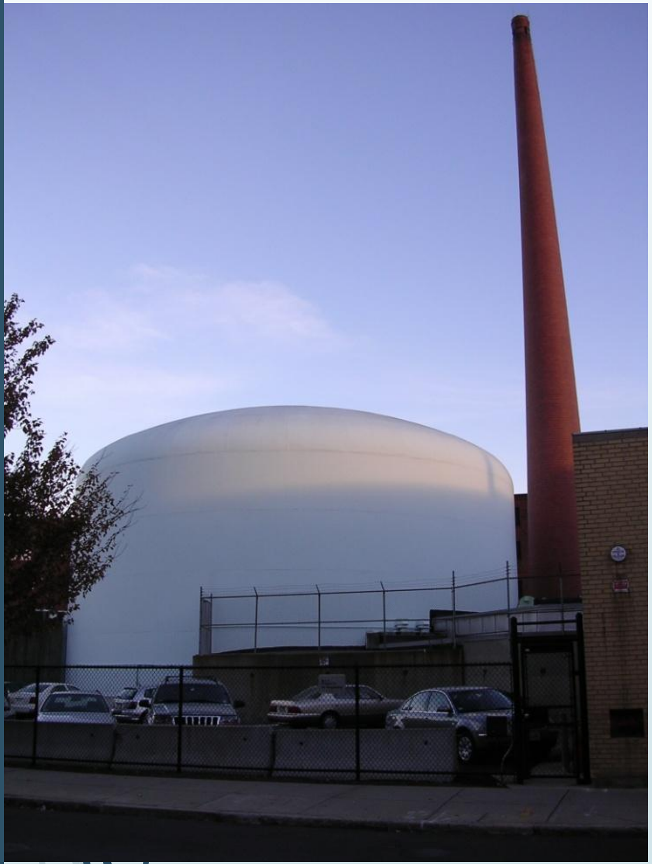
Neutron sources for BNCT: Beam Shaping Assembly

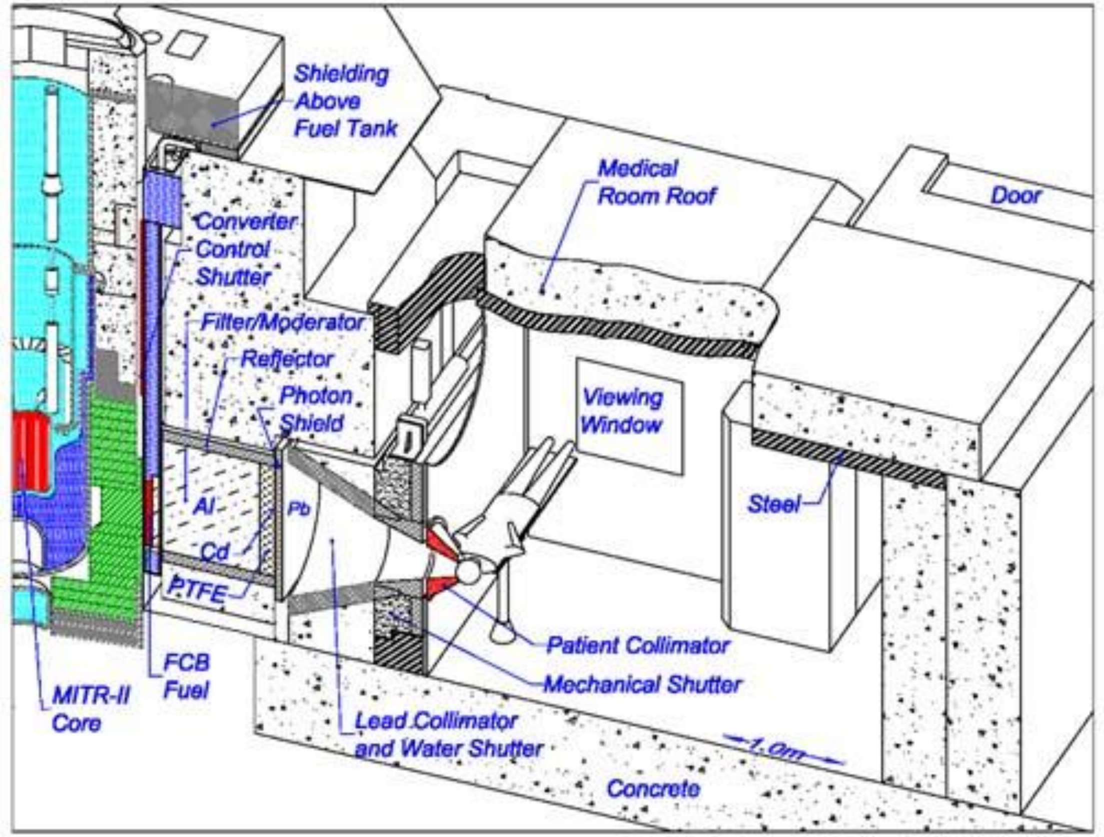
Kyoto Research Reactor



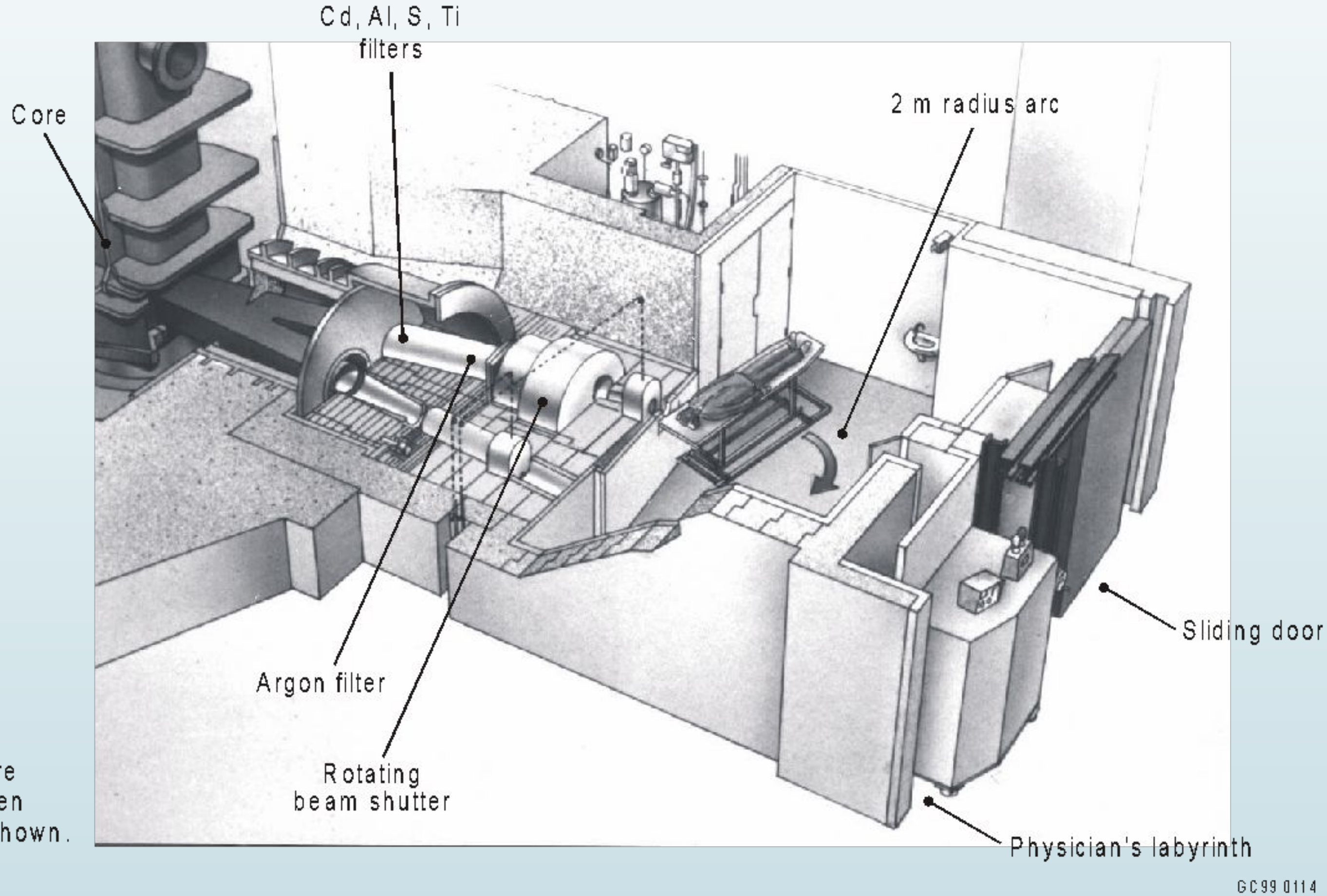


Harvard MIT reactor USA





Overall view of the Petten BNCT Therapy Facility



Note:
As an aid to clarity, all but four of the bottom layer of 100 mm square steel, roof shielding bars have been omitted. Polybor linings are not shown.

(Illustration provided by the Joint Research Centre, Petten)

Cross-Sectional View of Neutron Beam facility, JRR4.

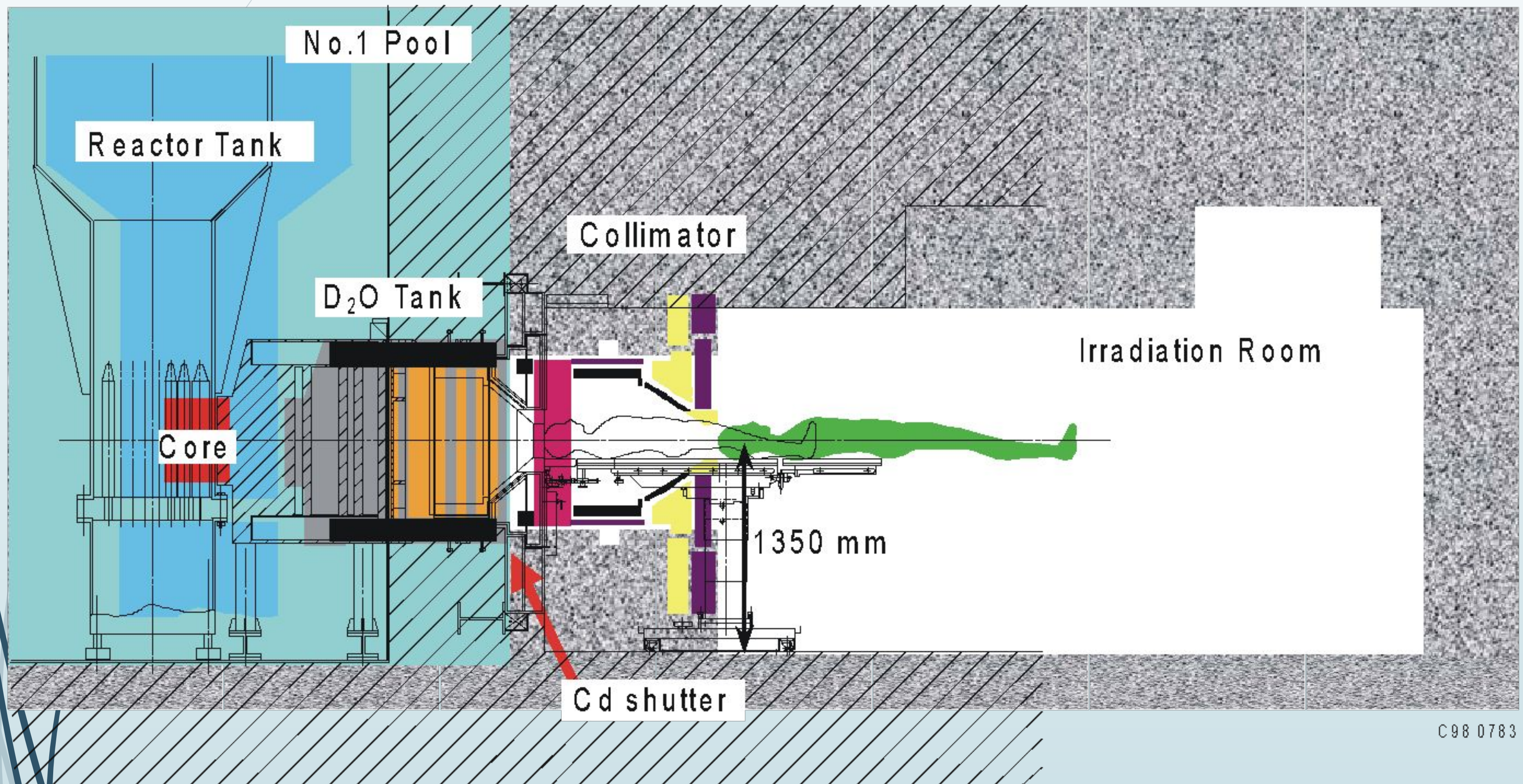


Illustration provided by the Japanese Atomic Energy Research Institute

ARGENTINA?

ITALY?

TRIGA MARK II REACTOR AT LENA

Steady-state power: 250 kW

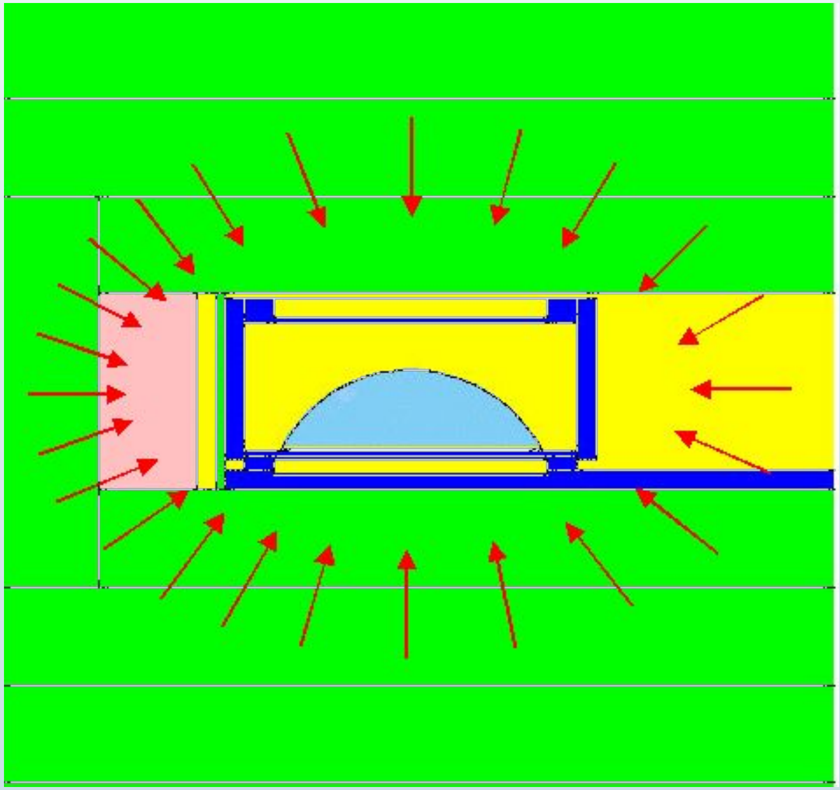
Extra-corporeal liver BNCT for diffused metastases

TAOrMINA project

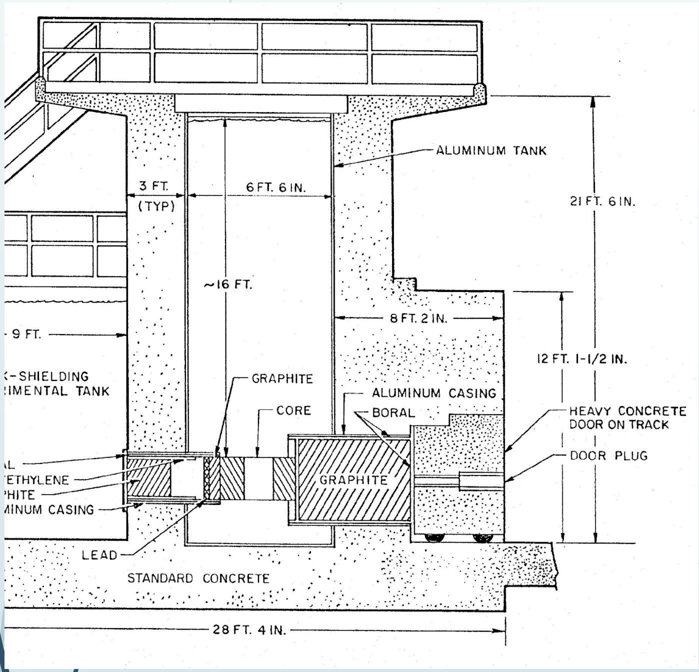
Trattamento Avanzato Organi Mediante Irraggiamento Neutronico e Autotrapianto

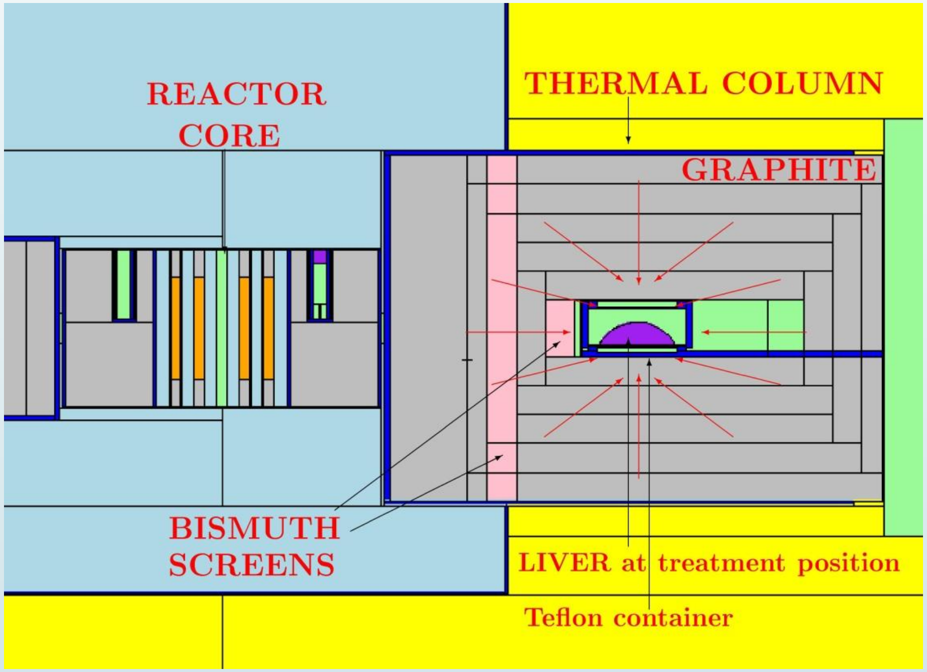
Advanced Treatment of Organs by Neutron Irradiation and Auto-graft

The treatment is based on the irradiation of the isolated organ in a neutron field where neutrons coming from all directions can irradiate the whole liver

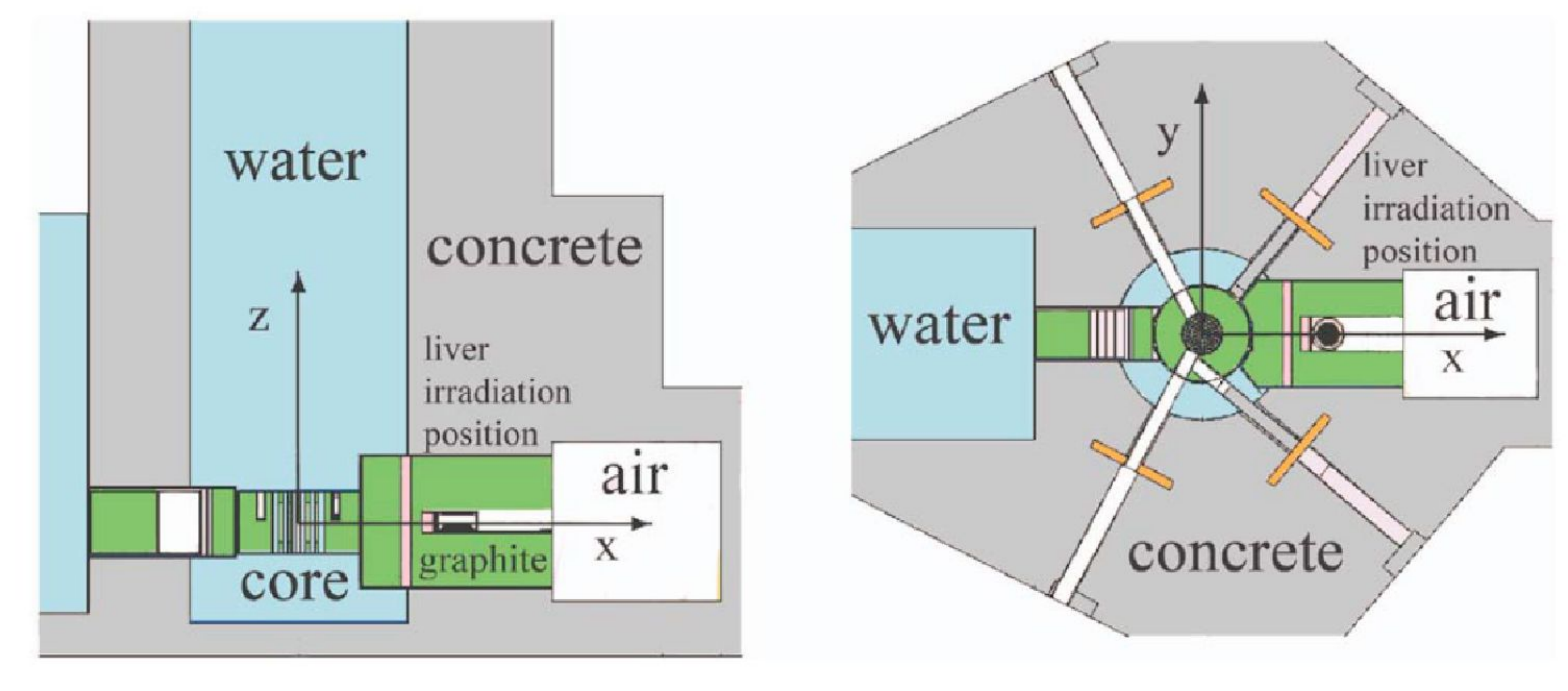


THERMAL COLUMN MODIFICATION
for liver irradiation





The irradiation facility characterization



MCNP geometry
Vertical and horizontal section of Pavia Triga Mark II reactor

The irradiation facility charachterization

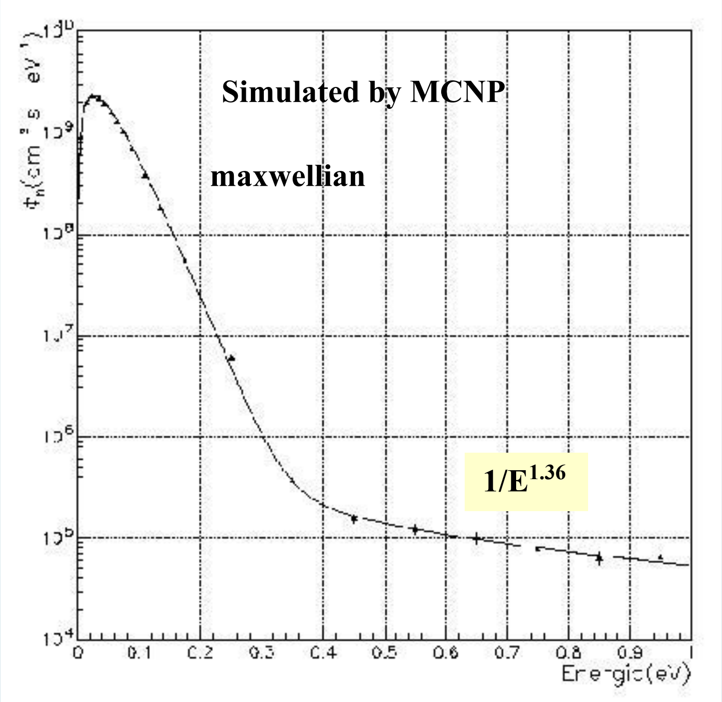
Neutron flux at liver irradiation

$$\phi_{th} = 1.4 \cdot 10^{10} cm^{-2} s^{-1} (E_n < 0.2 eV)$$

$$\phi_{epi} = 3.3 \cdot 10^{7} cm^{-2} s^{-1} (0.2 eV < E_n < 3.5 MeV)$$

$$\phi_{fast} = 2.0 \cdot 10^{6} cm^{-2} s^{-1} (E_n > 3.5 MeV)$$

$$\phi_{fast} = 9.4 \cdot 10^{4} cm^{-2} s^{-1} (E_n > 8.2 MeV)$$



Neutron flux in liver

MCNP geometry of the liver phantom inside the Teflon holder placed in the irradiation position

The 1 cm3 voxels and the copper wires for thermal neutron measurement are visible.

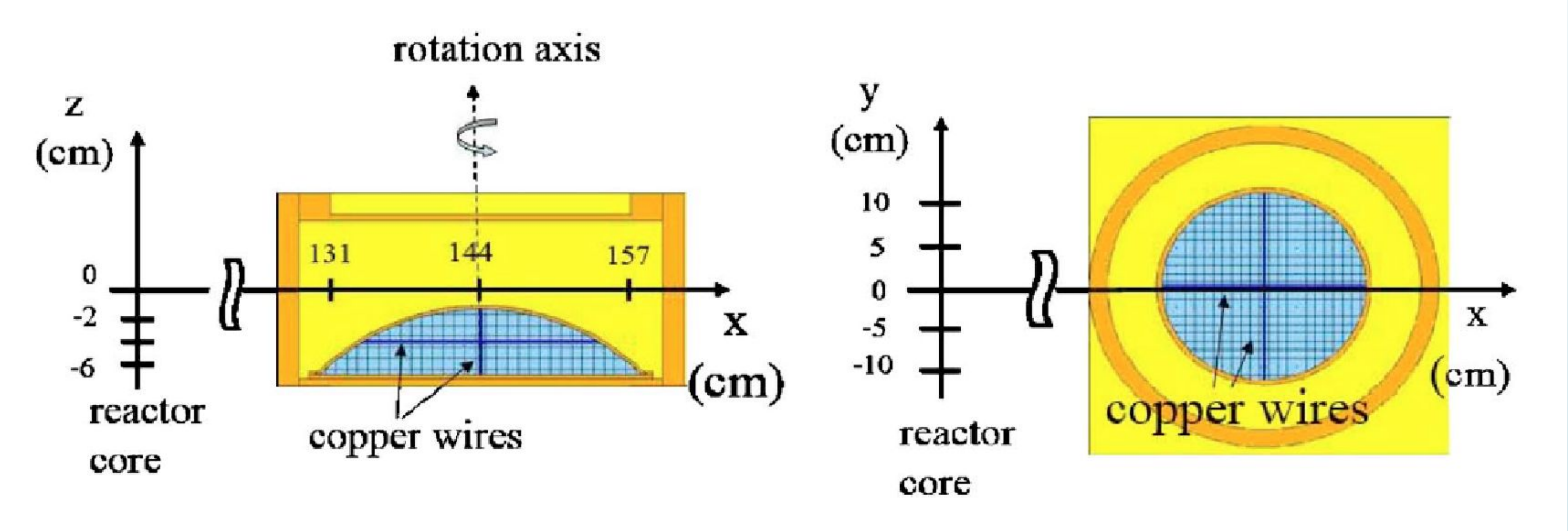
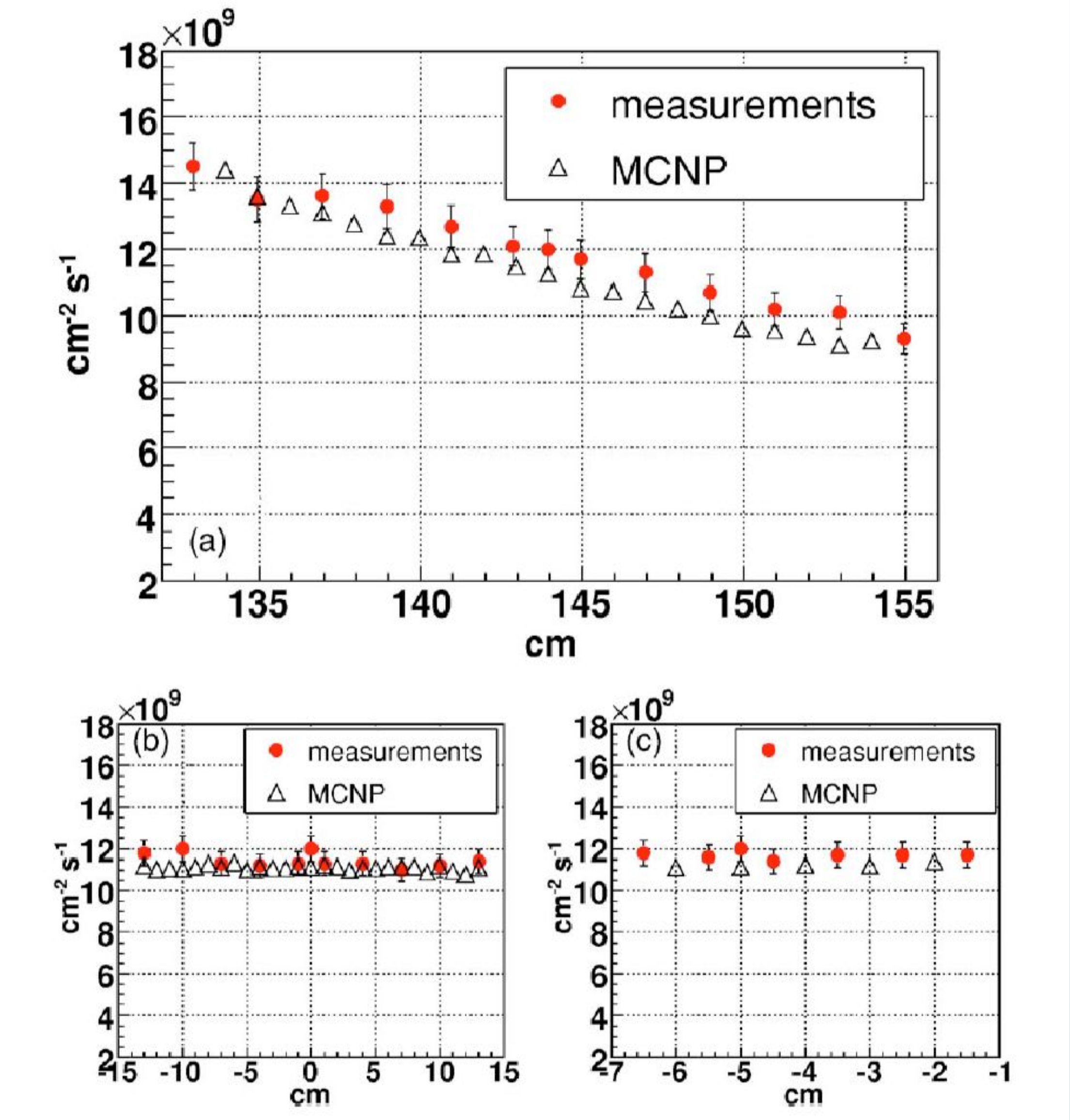


TABLE II. Elemental composition (% by weight) of the hepatic-equivalent solution compared to ICRU 46 liver composition (Ref. 14).

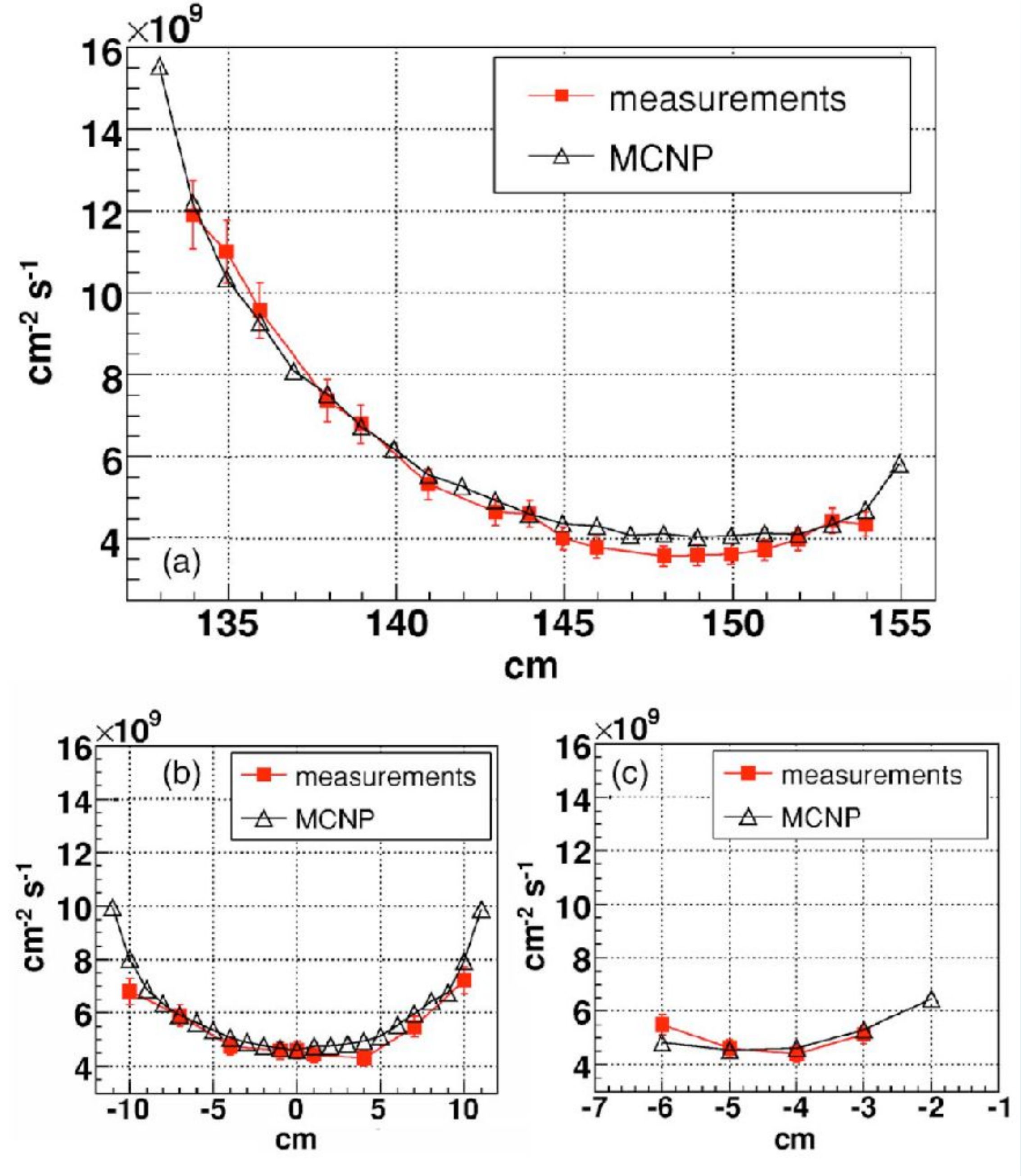
Element	O	C	H	N	P	K	S	Cl	Na
Liver ICRU 46	71.6	13.9	10.2	3.0	0.3	0.3	0.3	0.2	0.20
Hepatic solution	83.86	1.29	10.6	3.0	0.3	0.22	0.3	0.2	0.22

Neutron flux in liver



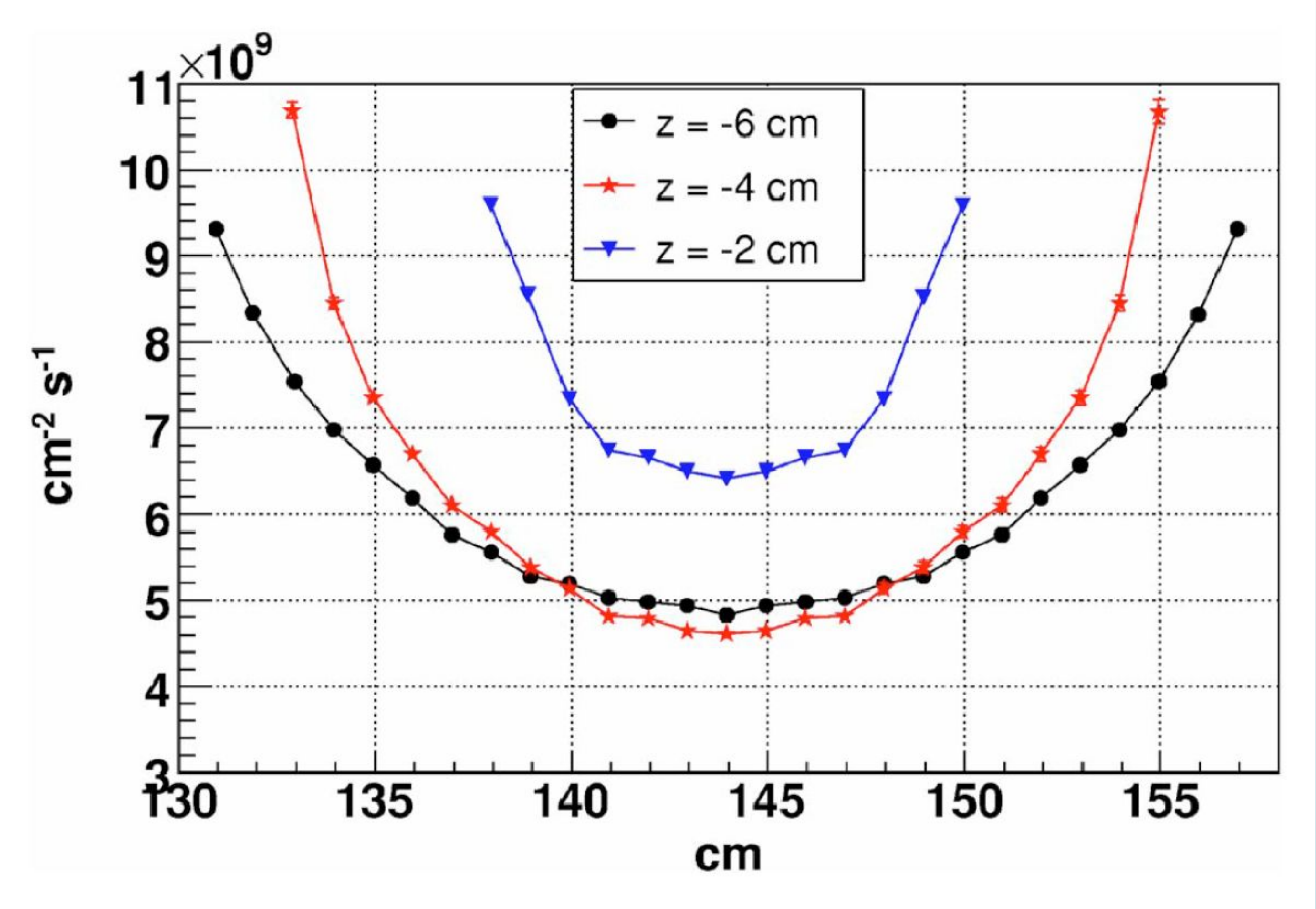
Thermal neutron flux distribution in the phantom filled with air along the *x*, *y* and *z* axes

Neutron flux in liver



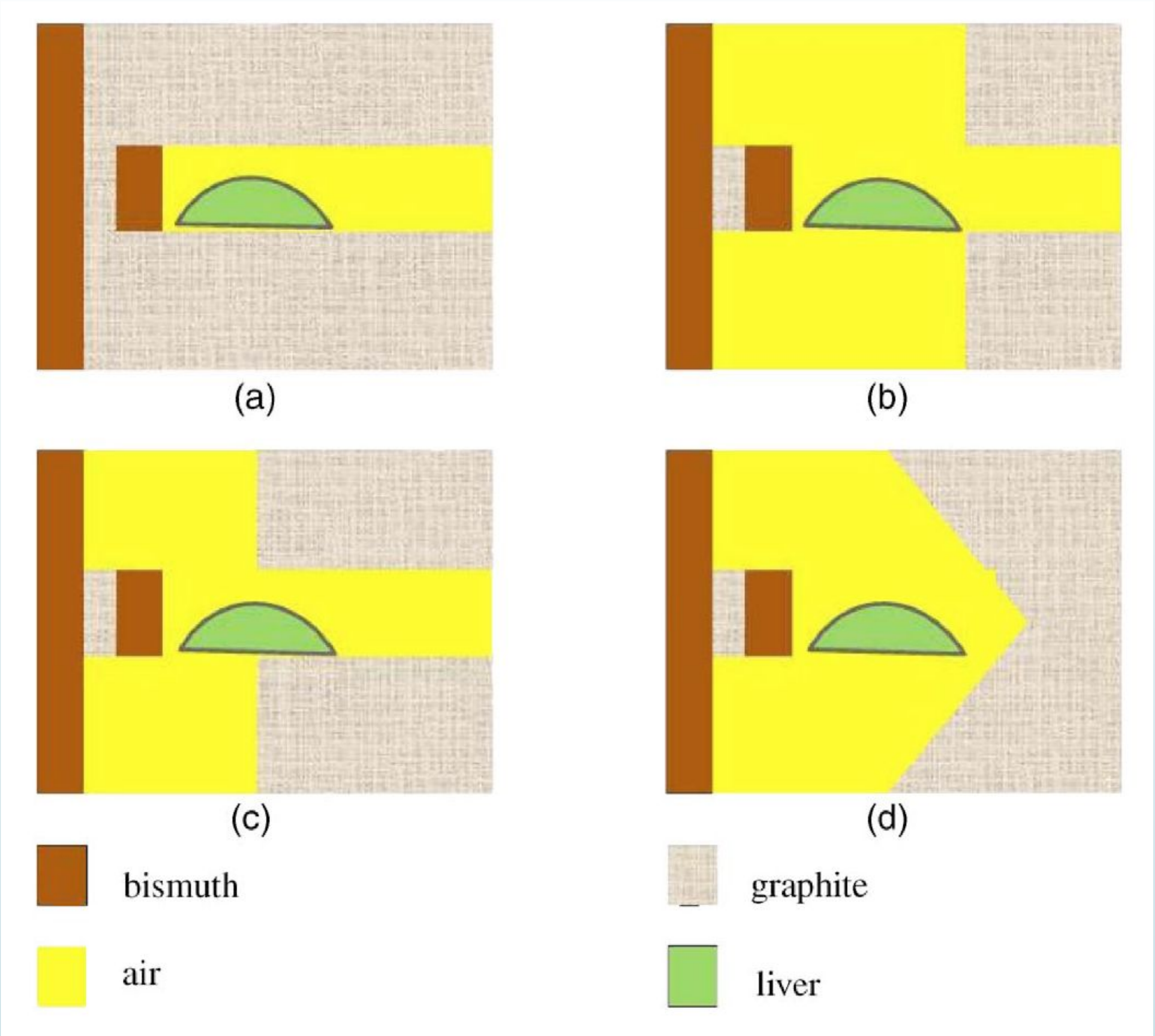
Thermal neutron flux distribution in the phantom filled with the hepatic-equivalent solution: along the *x*, *y* and *z axes*

Neutron flux in liver after rotation



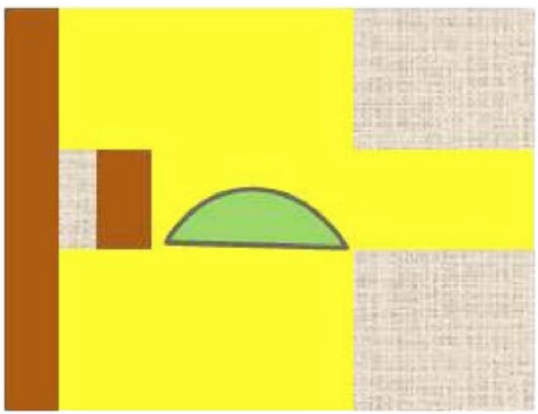
Calculated thermal neutron flux distribution along the longitudinal *x* axis after rotation of 180° at different positions along the *z* axis;

Trying to flatten the neutron flux in liver

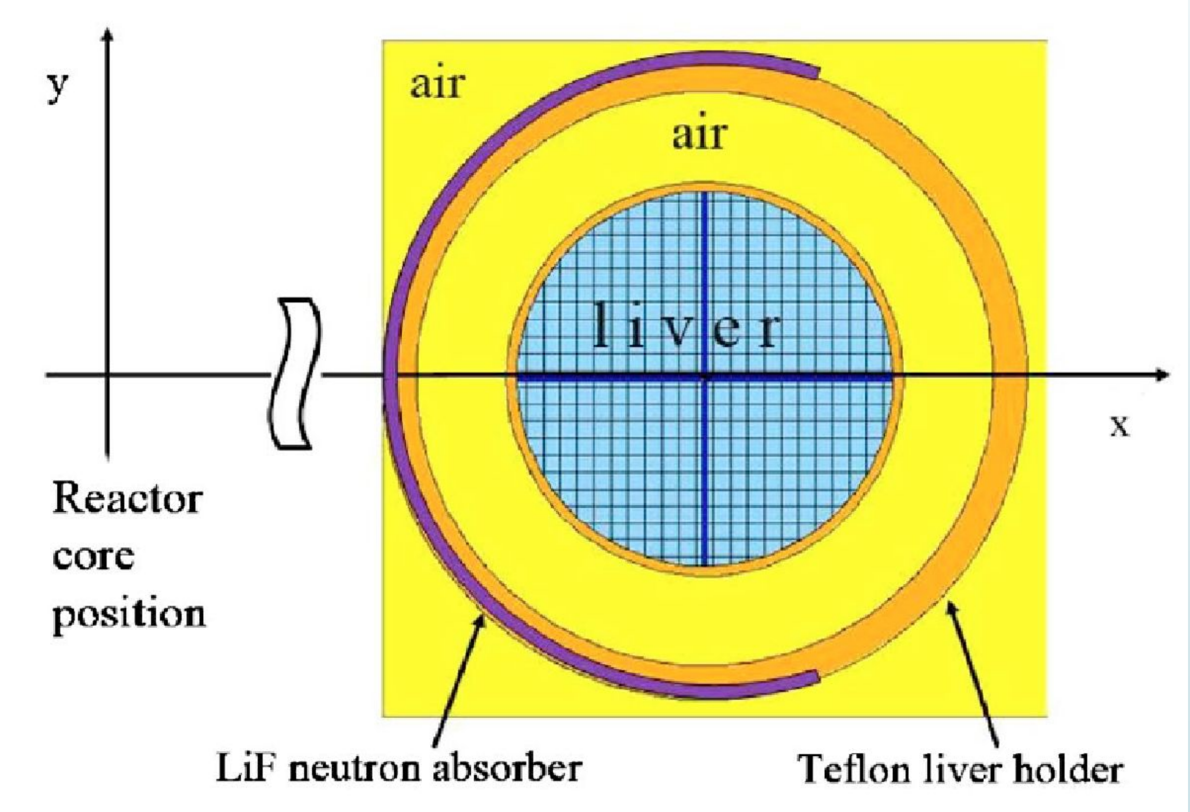


The different configurations tested were: a) the existing configuration used in patient treatment; b) larger open configuration; c) smaller open configuration; and d closed conical-shaped channel configuration.

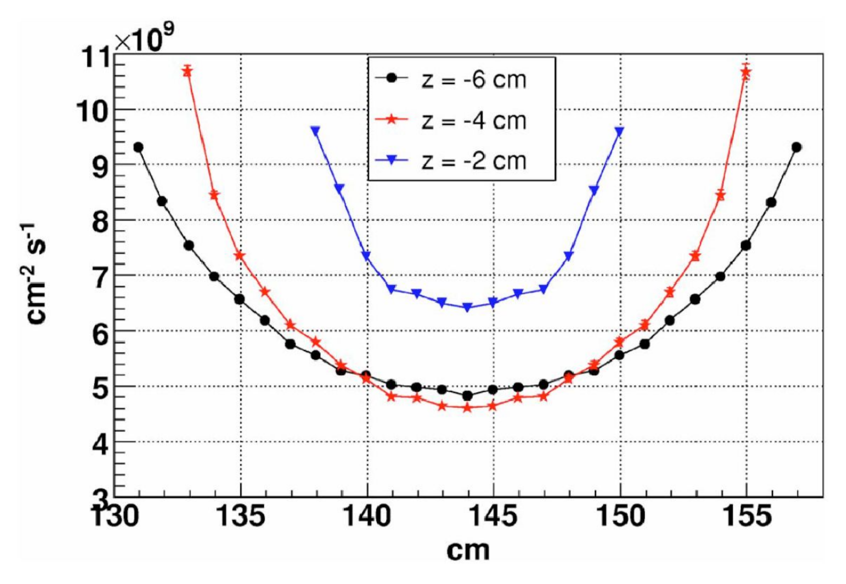
Trying to flatten the neutron flux in liver



(b)

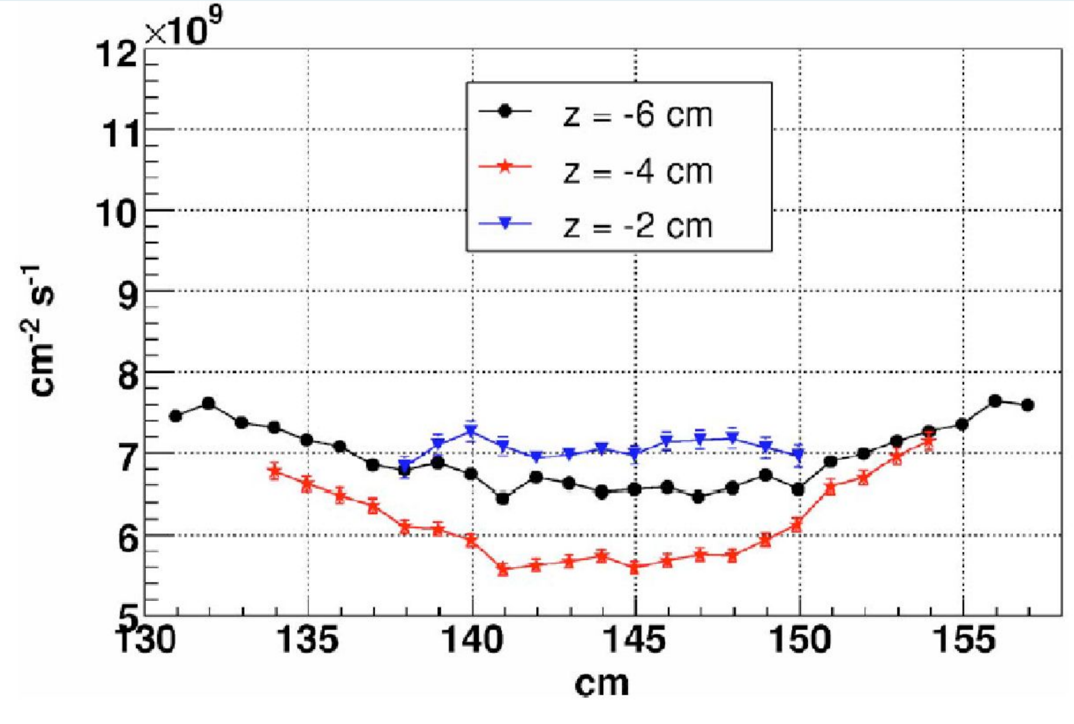


Trying to flatten the neutron flux in liver



with rotation

without rotation

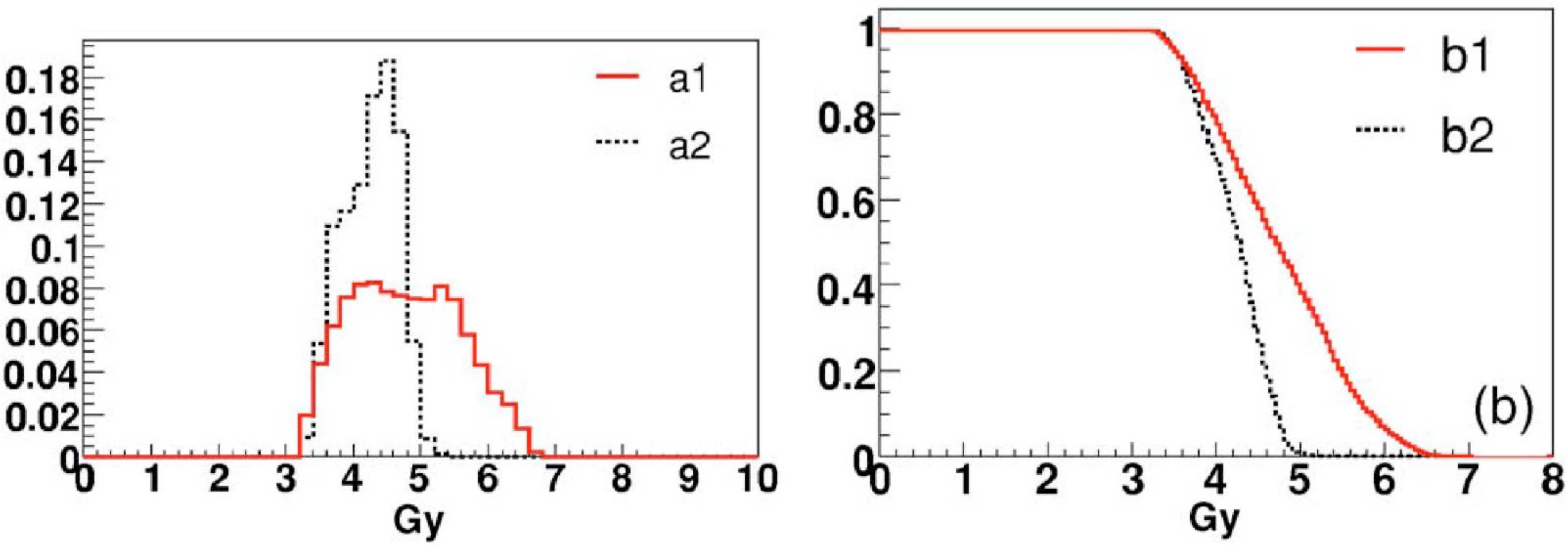


Dose distribution in liver

For calculations, the following conditions were assumed:

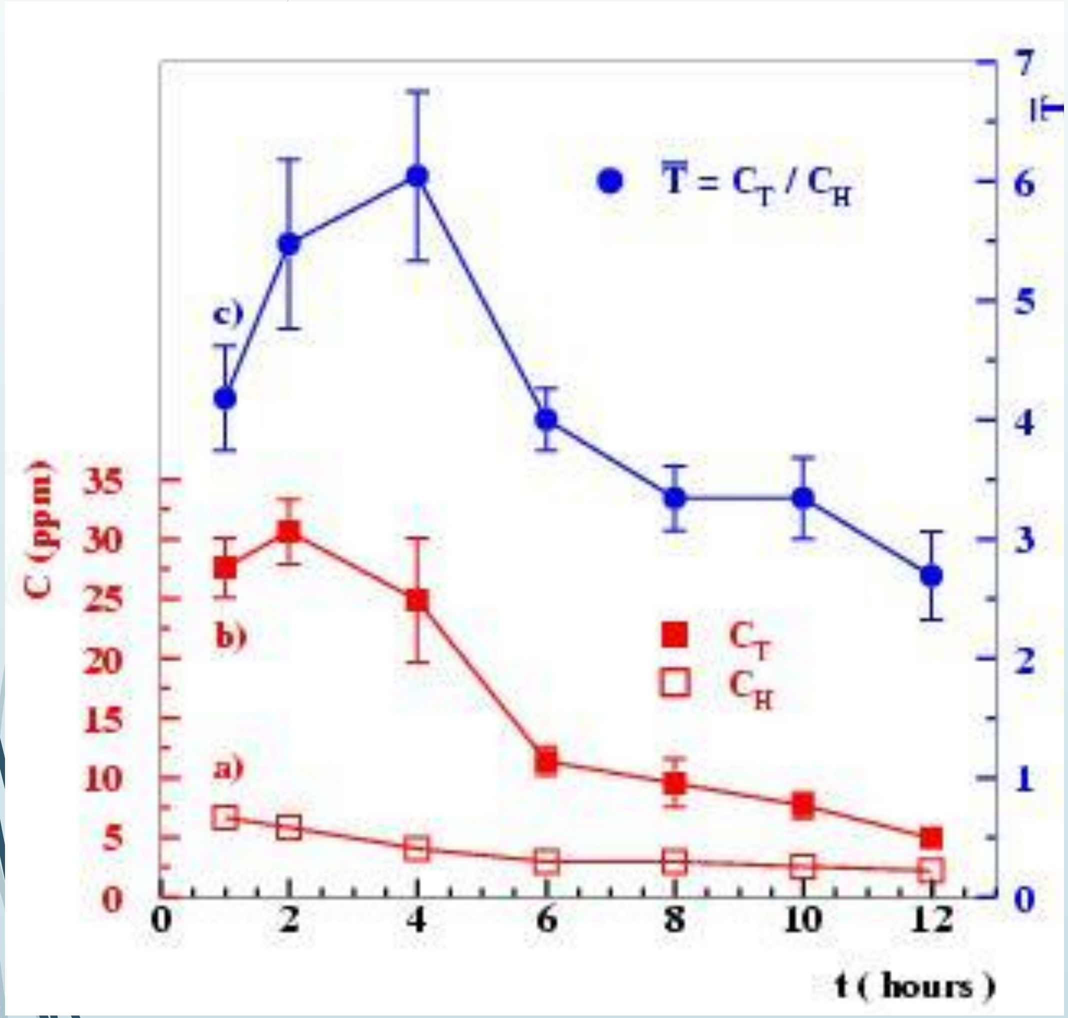
(1) ^{10}B concentration of 8 ppm in the healthy liver;
(2) ^{10}B concentration of 50 ppm in the tumor;
(3) an irradiation time T_{irr} to deliver a minimum thermal neutron fluence, $\Psi = 4 \times 10^{12}$ cm^{-2}, to the tumor. It was assumed that the tumor was located in voxels in which the thermal flux was at a minimum (Φ_{min}), thus: $T_{irr} = 4 \times 10^{12} / \Phi_{min}$.

tumor dose > 17 Gy,
healthy dose < 7 Gy.



Differential DVH and integral DVH for graphite configuration
in the actual facility and for the configuration b) with LiF absorber

Boron up-take: in the animal model



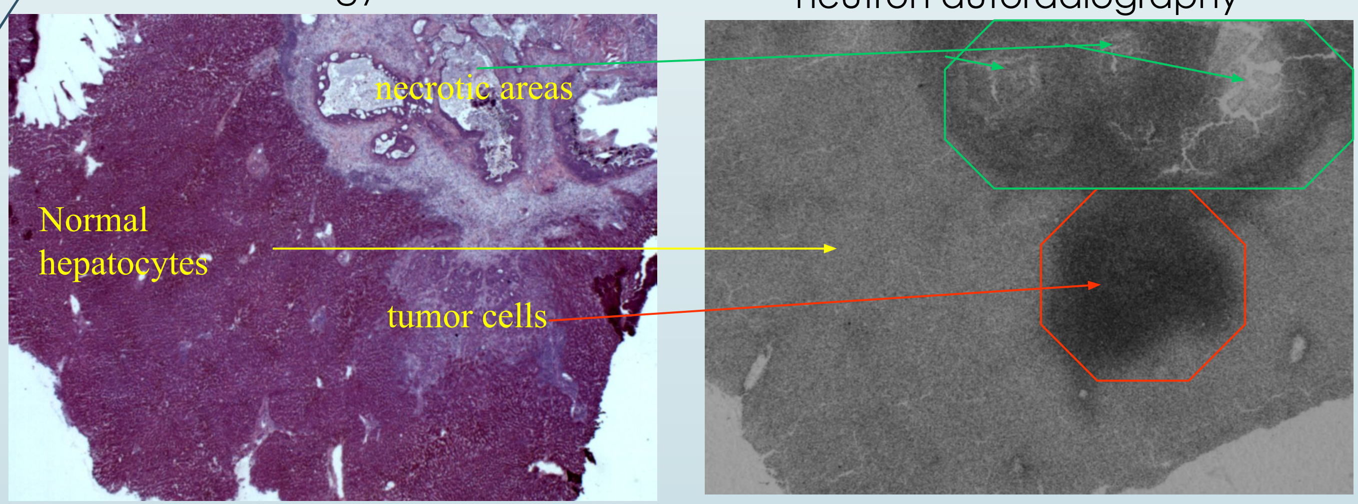
In the time interval from 2 to 4 hours after BPA perfusion the boron concentration in tumour (CT) presents the highest values and the ratio of boron concentration in tumor over normal tissue (T) is at the maximum value of 6

Boron up-take: in patients

BPA was administered at a dose of 300 mg/Kg body weight, during surgery, through a colic vein; the infusion was 2 hours long. To measure Boron concentration some biopsies were taken both from healthy and tumour tissues. Alpha Spectrometry and Neutron Autoradiography showed a selective Boron absorption in metastases (50 ppm in tumours and 8 ppm in liver tissue)

histology

neutron autoradiography



Liver coming out from the patient's body

Liver-out

Liver washing and refrigeration

Teflon bag




Refrigerated teflon container

At the reactor thermal column

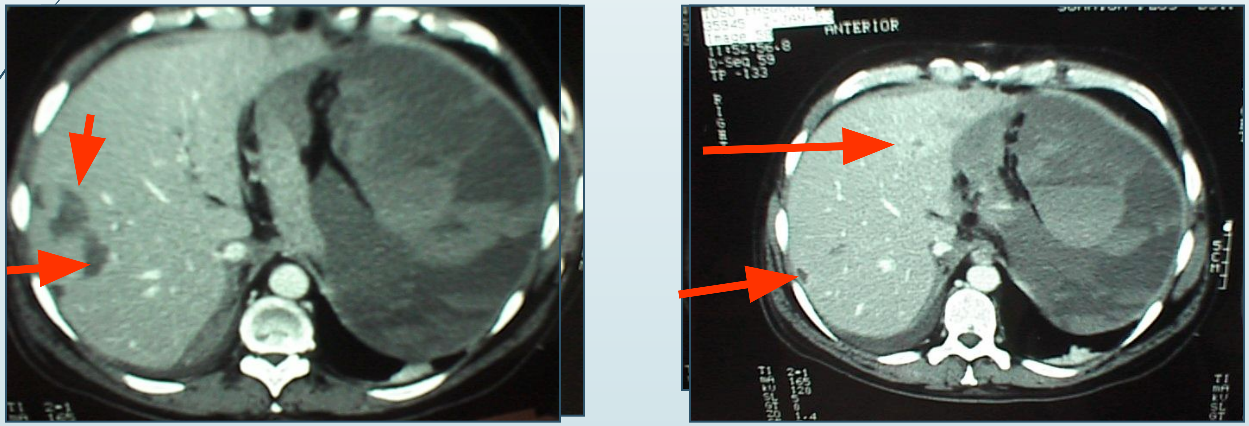
Pushing the liver into the reactor

Pushing the liver into the reactor

Back to the surgery room

CT scan after BNCT

7 days after treatment the CT scanning evidenced the liver in normal condition while the metastases appeared in a necrotic state



Arrows indicate the necrotic zones detected after the neuton irradiation

Patients treated

Two terminal patients affected with liver metastases were treated in Pavia with the TAOrMINA method.

"The first patient (TP) was a male, 48 years old, with 14 syncronous metastases of a colon carcinoma operated 7 months before. The residual liver function as expressed by galactose elimination capacity (GEC) was 63% (normal values >70%). The operation was performed in December 2001. …

The second patient (TS) was a male, 39, with 11 large syncronous bilobar metastases in the liver from a rectal carcinoma resected 9 months before. He was also suffering from a dilatative cardiomiopathy with a stroke volume of 40% (n:v.>50%): the cardiac function was been worsened by the chemiotherapeutic regimen he followed before BNCT, liver function (GEC) was 58% …

A. Zonta et al., doi:10.1088/1742-6596/41/1/054

The outcome of the treatment

The outcome was different in the two patients.

The second patient who experienced also a vascular complication … was reoperated in the 31st post-operative day, but a sudden cardiac failure determined his death in the 33rd p.o.day.

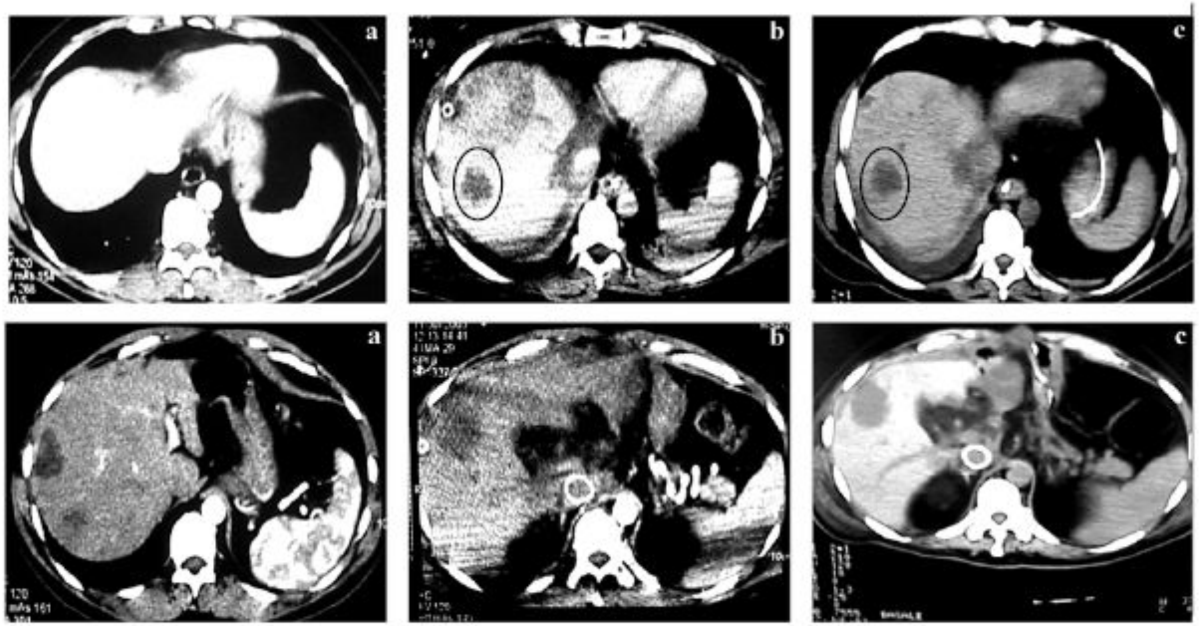


Figure 7. Modification of CT images of the liver on a cranial (above) and a caudal (below) level in the second patient from (a) the pre-operative aspect up to the situation (b) at 10 days and (c) at 21 days during the peri-operative follow-up after BNCT. In the (b) and (c) images of the upper row, an area of necrosis is encircled, not corresponding in the preoperative scan (a) to any known metastasis

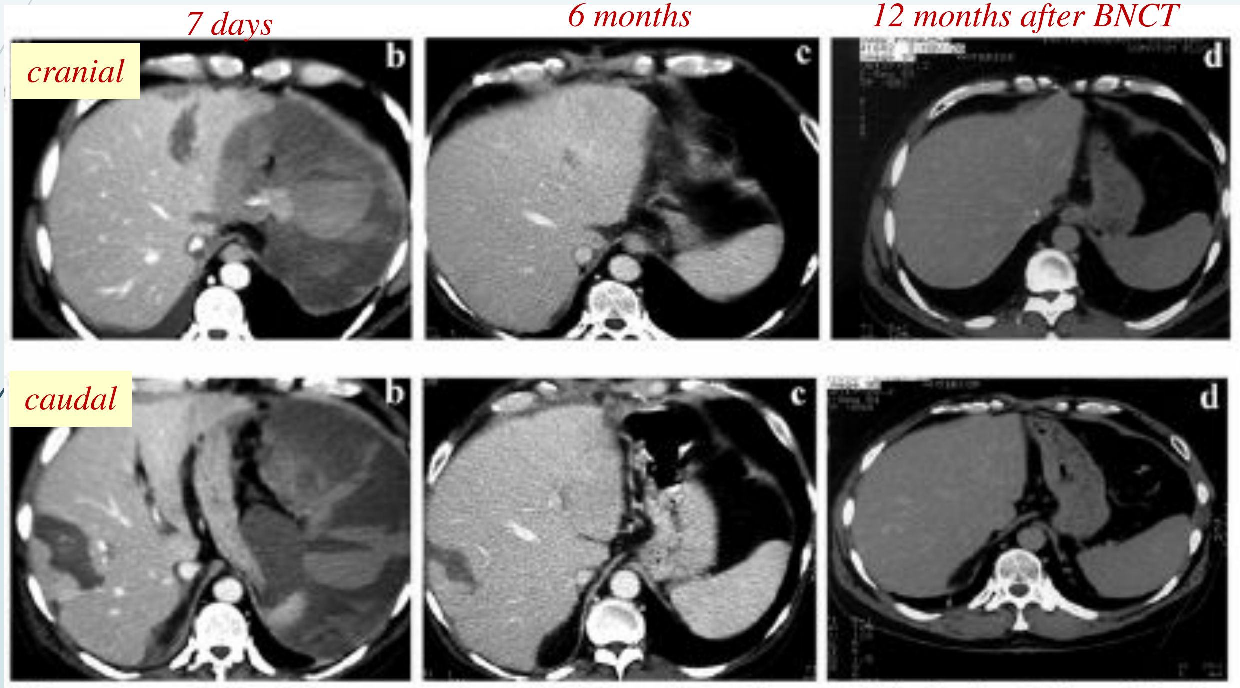
The outcome of the treatment

The outcome was different in the two patients.

In the first patient all clinical anomalies and biochemical alterations disappeared within some weeks and the patient was discharged in the 40th p.o.day.

Before leaving the Polyclinic he recovered all of his functions and his general condition was good.

The outcome of the treatment



Sequence of CT images of liver in the first patient subject to BNCT. Evolution at different times of the metastases towards necrosis with final substitution by normal tissues

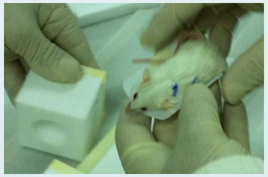
On Top of the reactor on April 2005

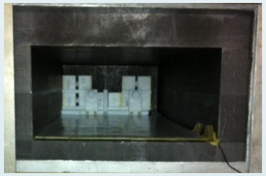
The control on April 2005 showed some recurrences inside and outside of liver He died on August 2005

He survived 44 months with a good quality of life; he died because of diffuse recurrences of his intestinal tumour

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 Thelluride

Installation of an accelerator based BNCT system in the Italian Hadron Therapy Center in Pavia

Thank
you