Radiation therapy of human glioma tumors experiments in SSTRC

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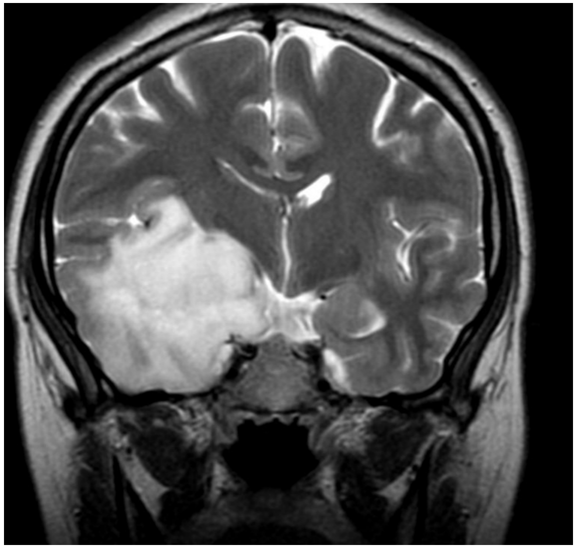
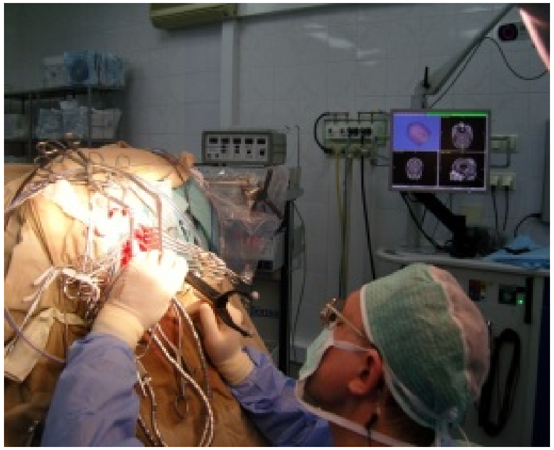
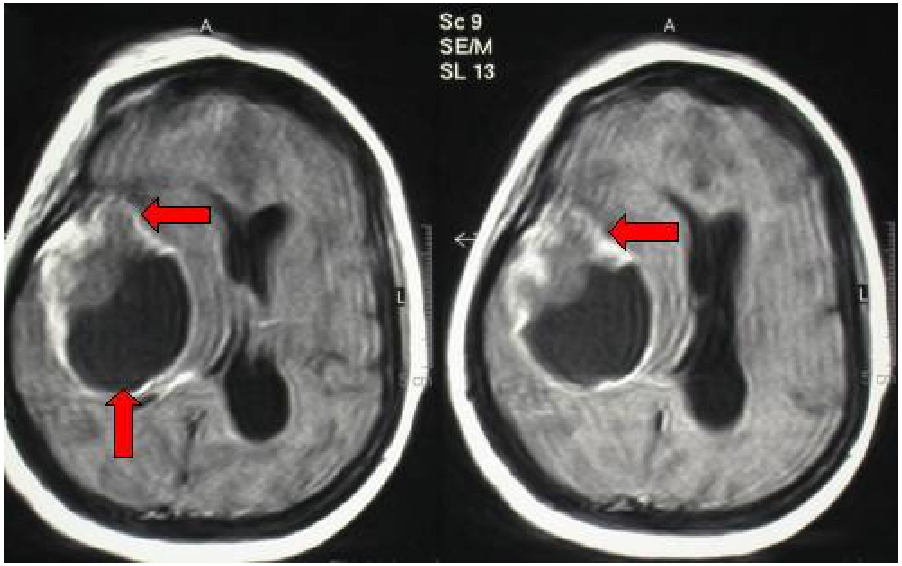
The human glioma tumors



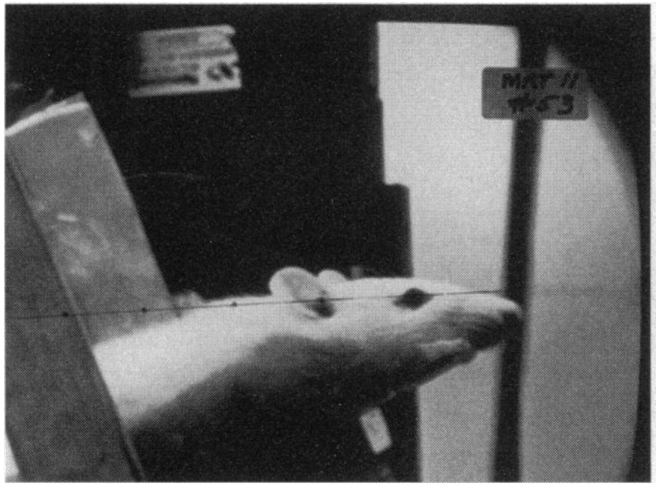
In modern society, brain diseases belong to most frequent causes of death. For prevention and treatment of neuropathology, a variety of therapeutic and surgical approaches are being developed and improved, including radiation therapy methods.

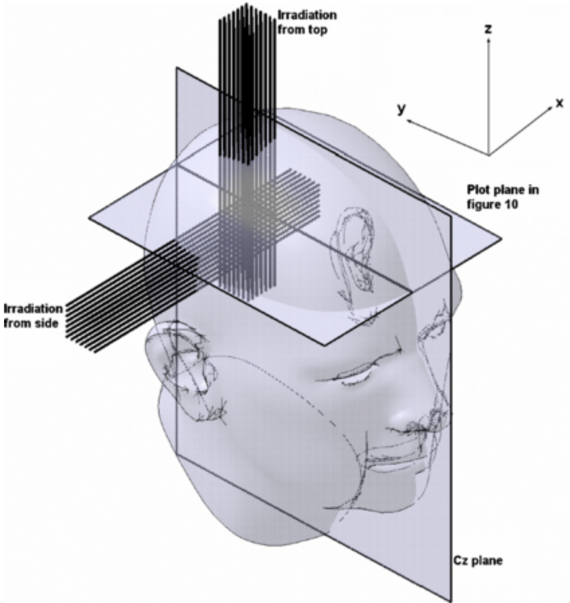


These methods have got a significant impetus to improvement through the creation of high-energy radiation sources and development of tools providing accurate targeting and strict time dosing in radiotherapy.



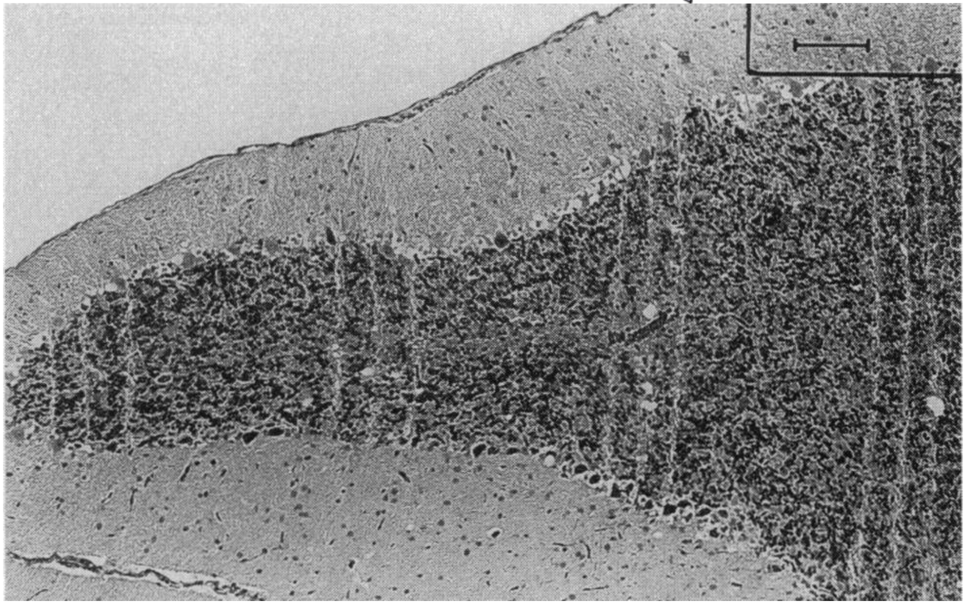
Microbeam radiation therapy



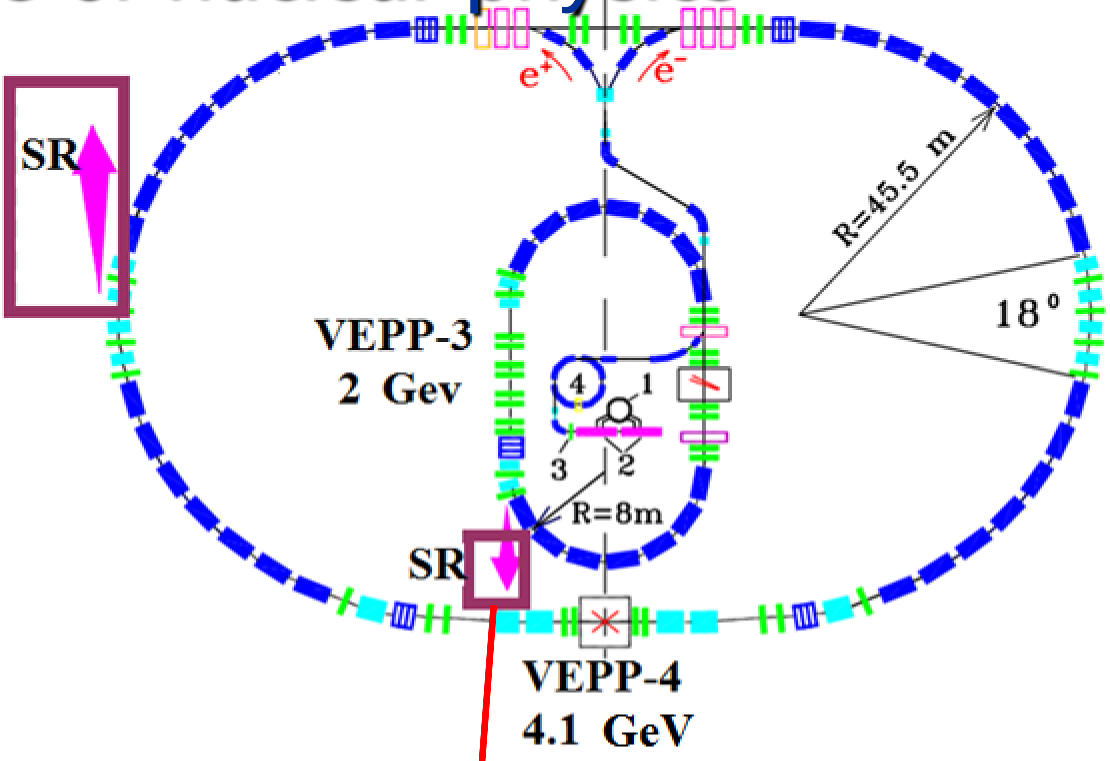


Subacute neuropathological effects of microplanar beams of x-rays from a synchrotron wiggler

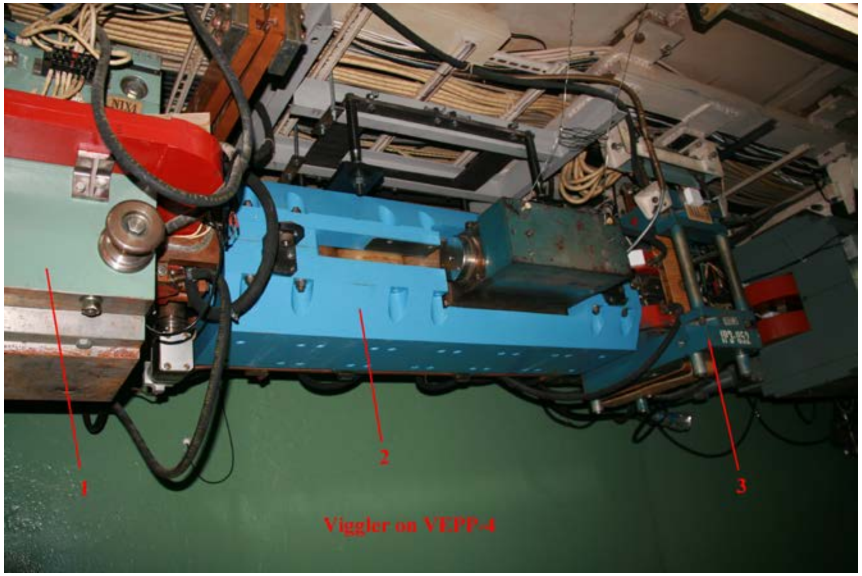
D. N. Slatkin, P. Spanne, F. A. Dilmanian, J.-O. Gebberst, J. A. Laissue



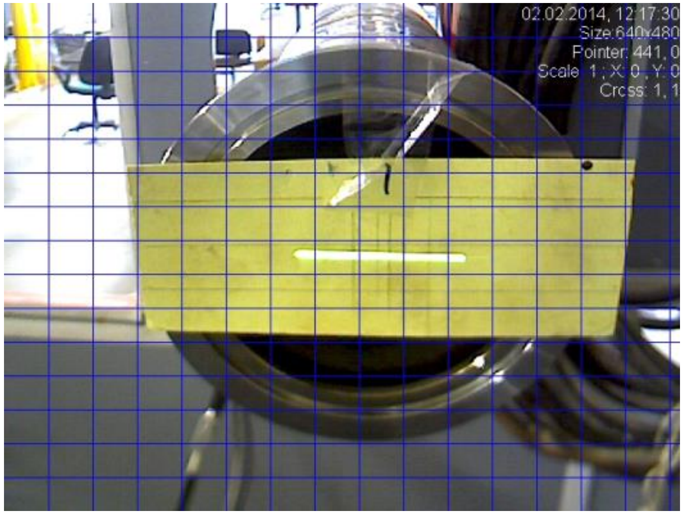
Synchrotron radiation sources in Novosibirsk Institute of nuclear physics

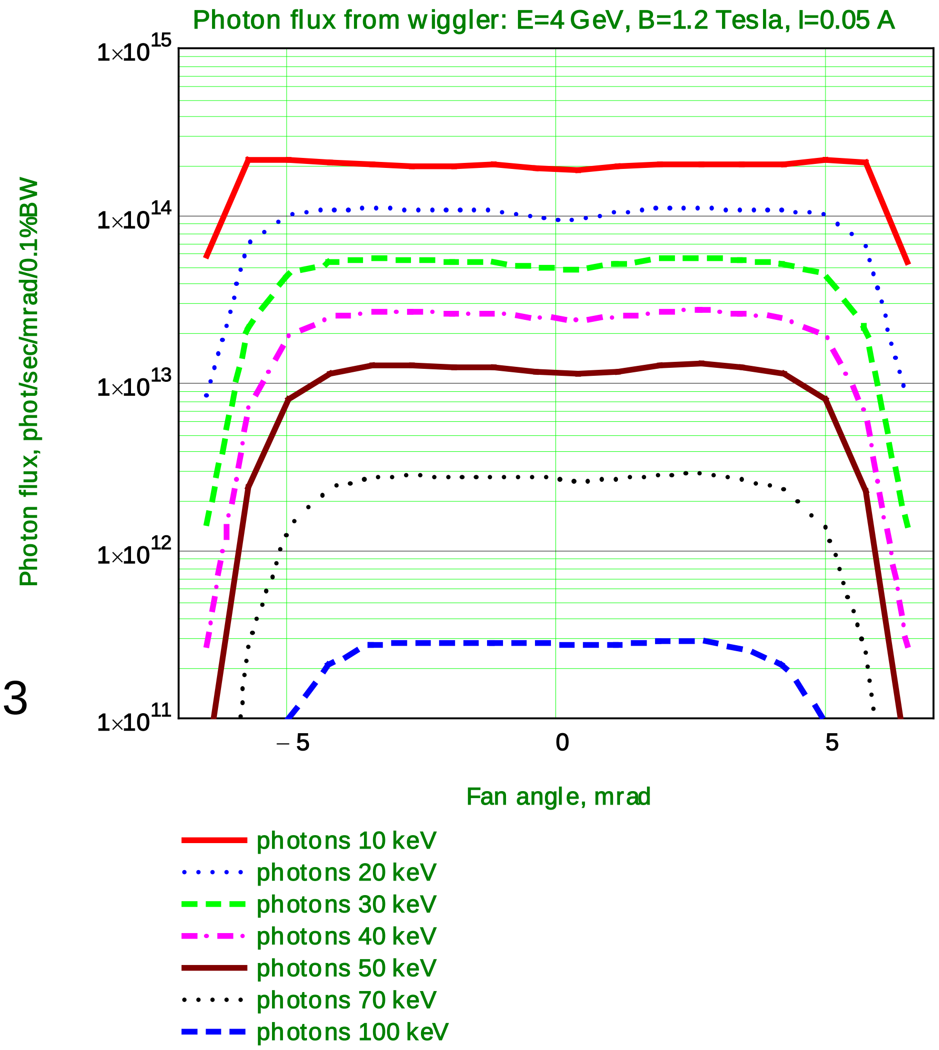


7 - pole wiggler was mounted at storage ring VEPP-4M



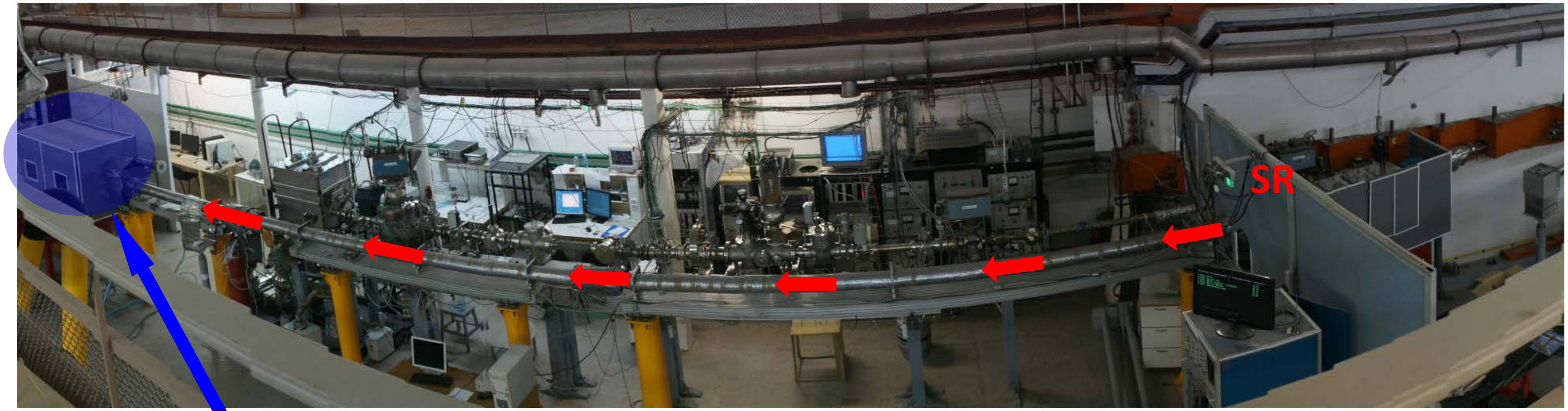
We got first beam from the wiggler in 2013



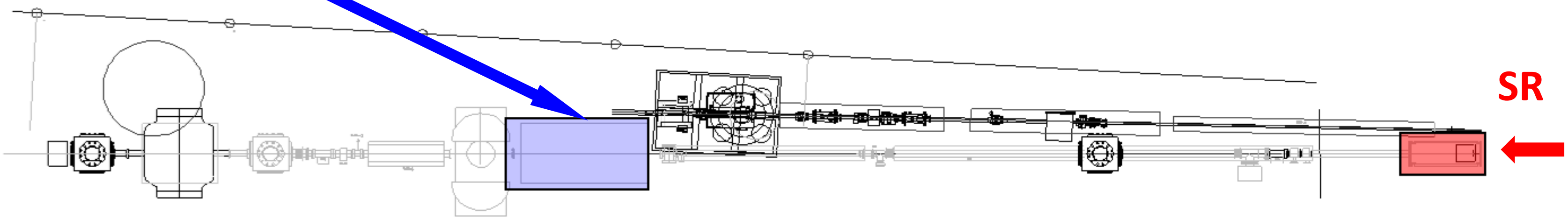


The angular flux distribution for different photons energies

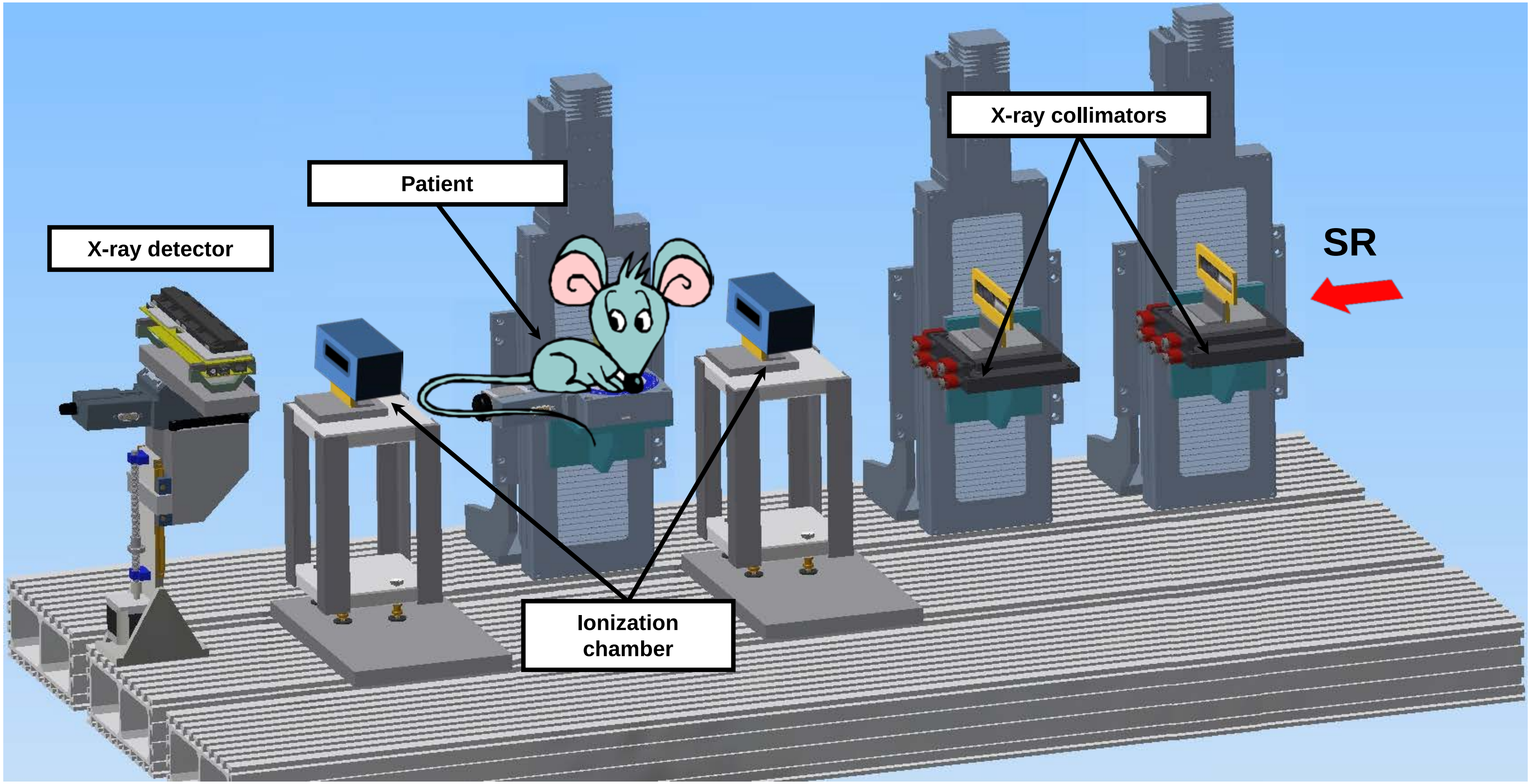
Beamline from 7 – pole wiggler



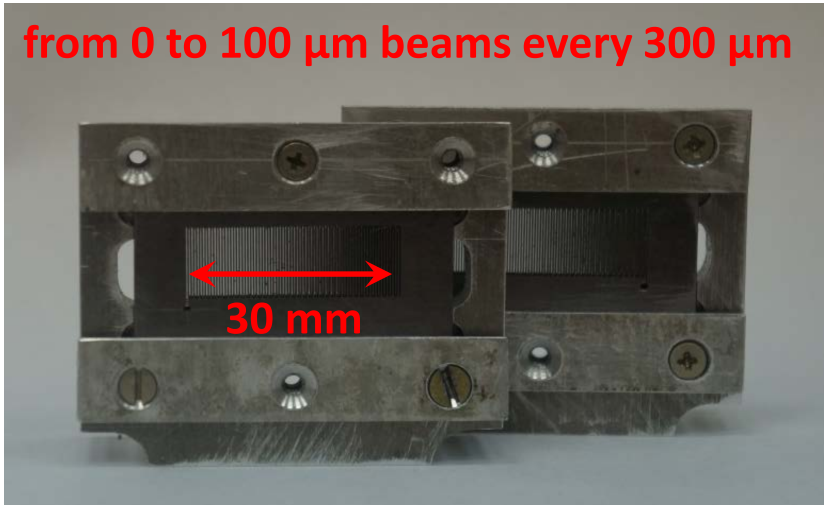
The experimental chamber located
32 m from irradiation source

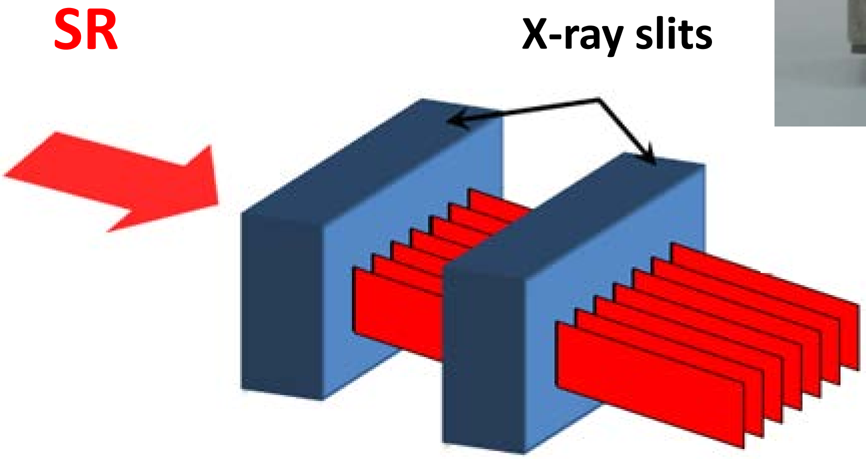


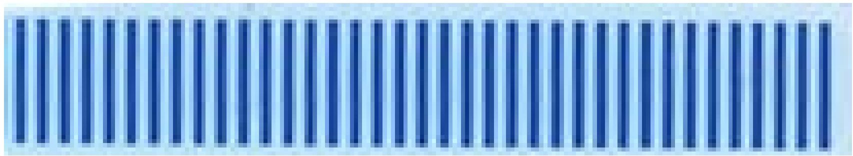
Layout for microbeam therapy experiments



Formation microbeams array by adjusting two X-ray slits

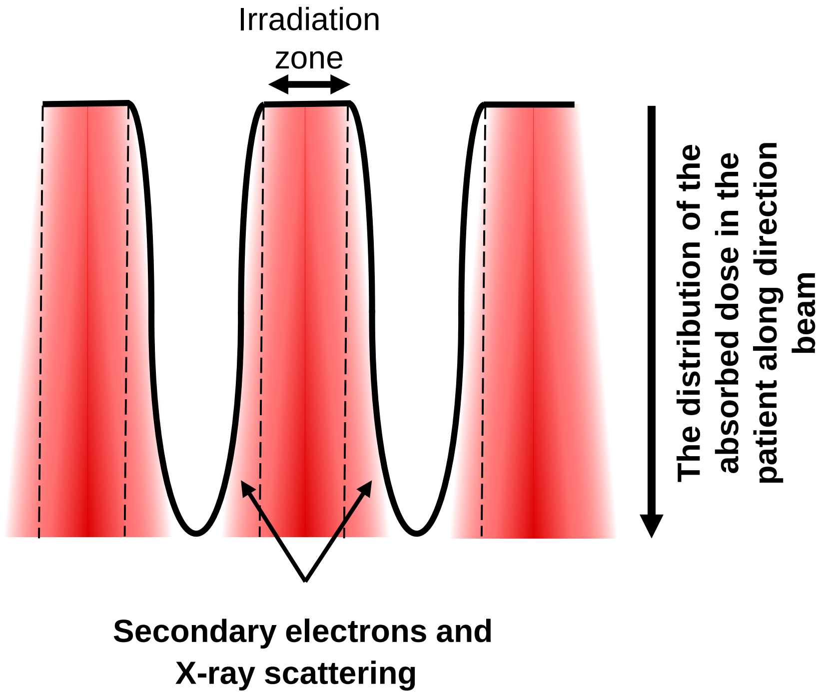






GAFCHROMIC® HD-810 Radiochromic Dosimetry Film

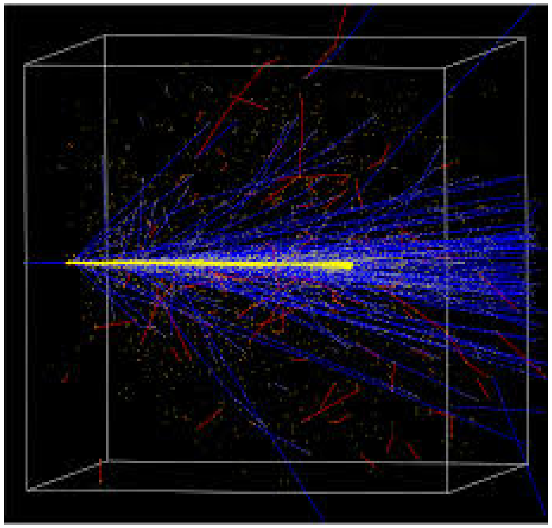
GEANT4 Monte Carlo simulation of beams array 100µm-wide incident on a water phantom

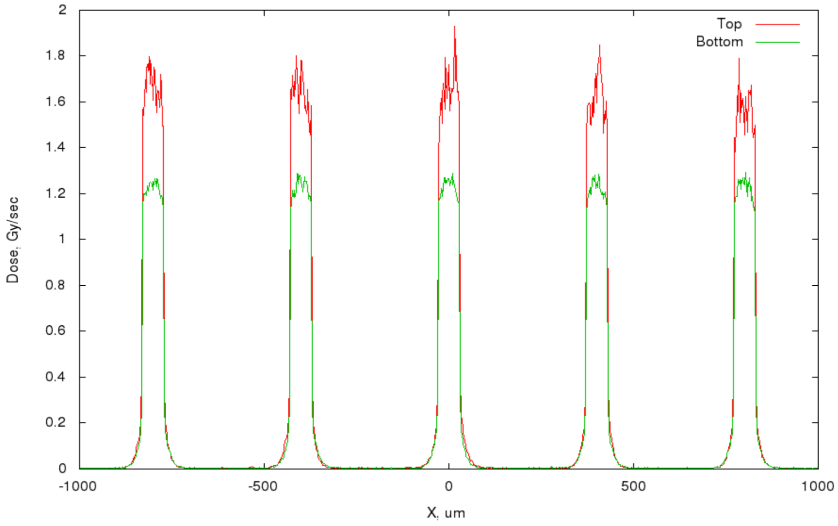


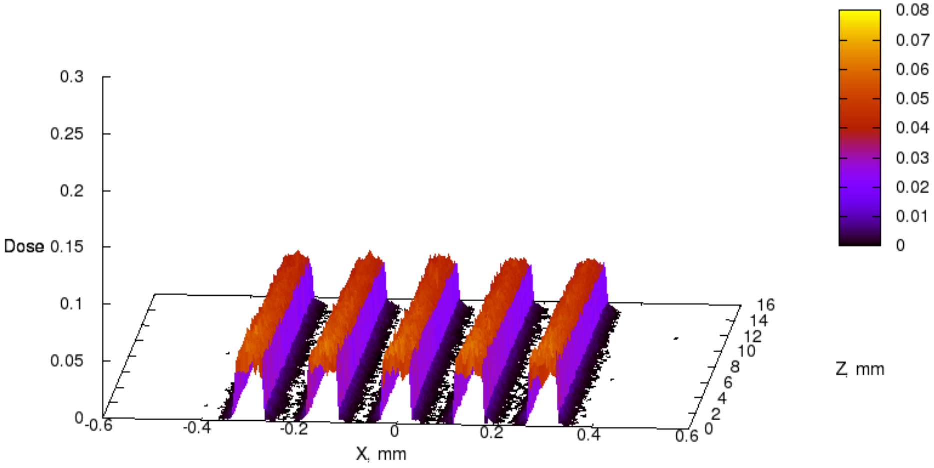
Irradiation zone

The distribution of the absorbed dose in the patient along direction beam

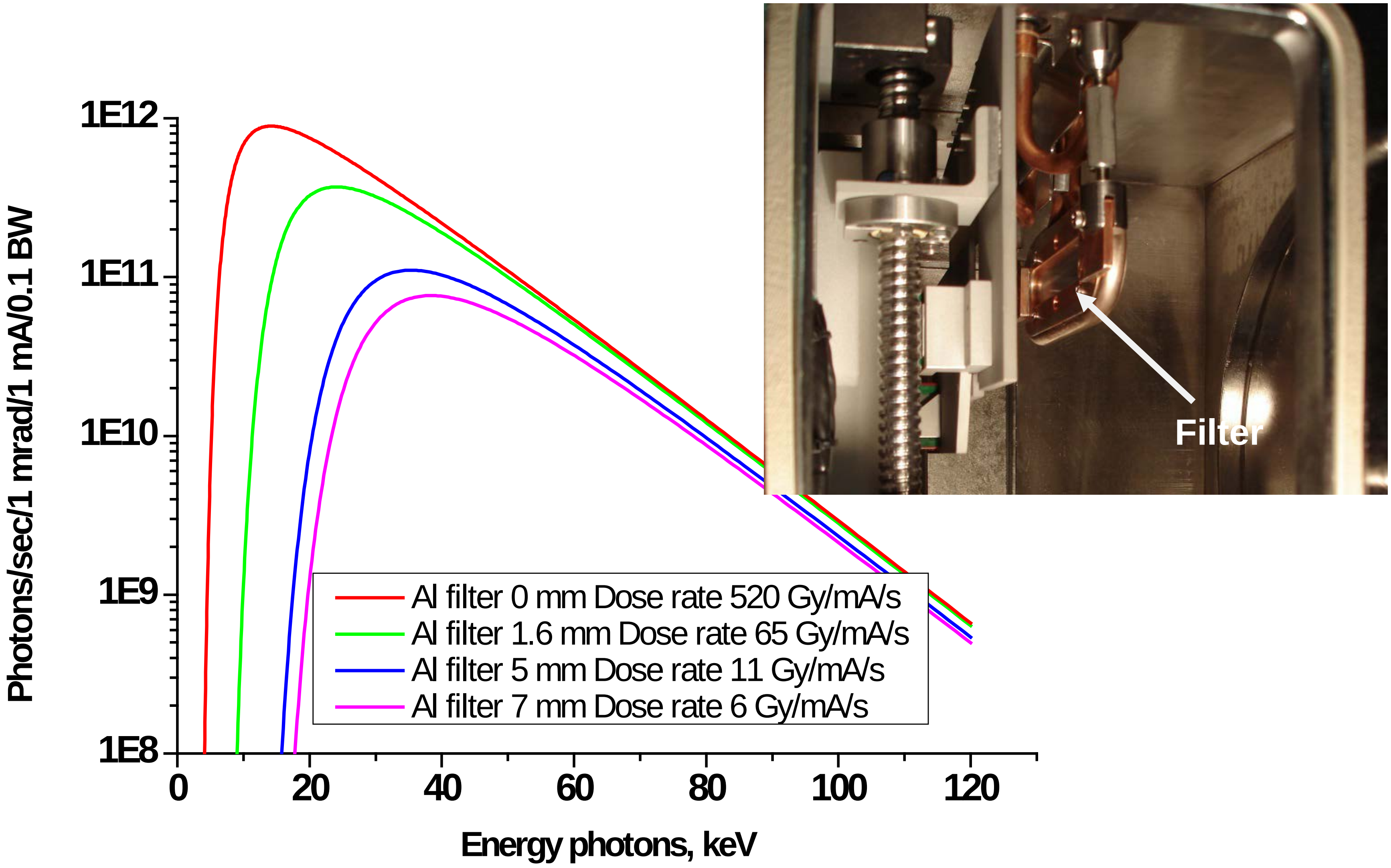
Secondary electrons and X-ray scattering



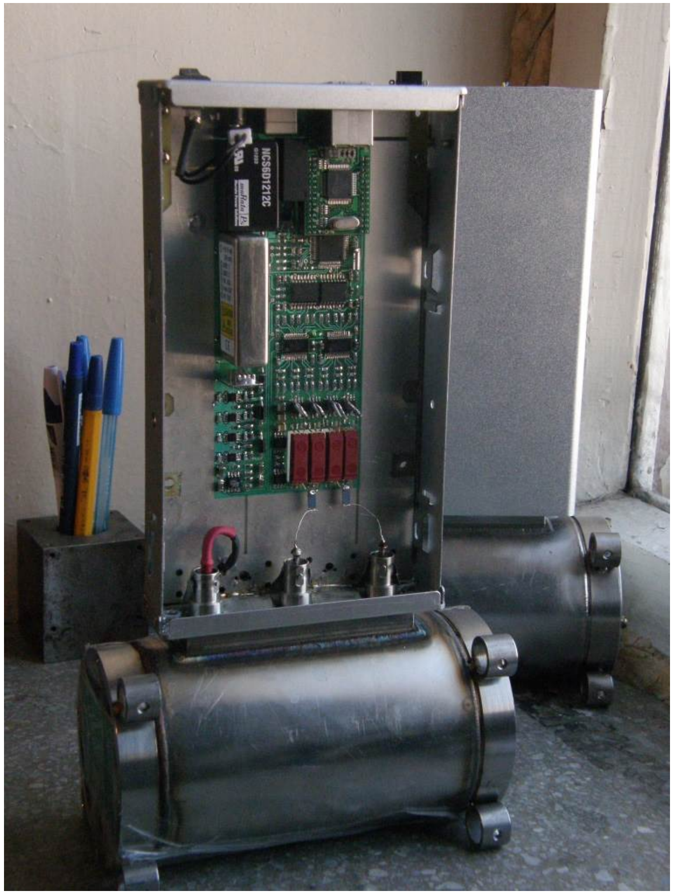




Dose rate and spectrum SR depending on filter thickness

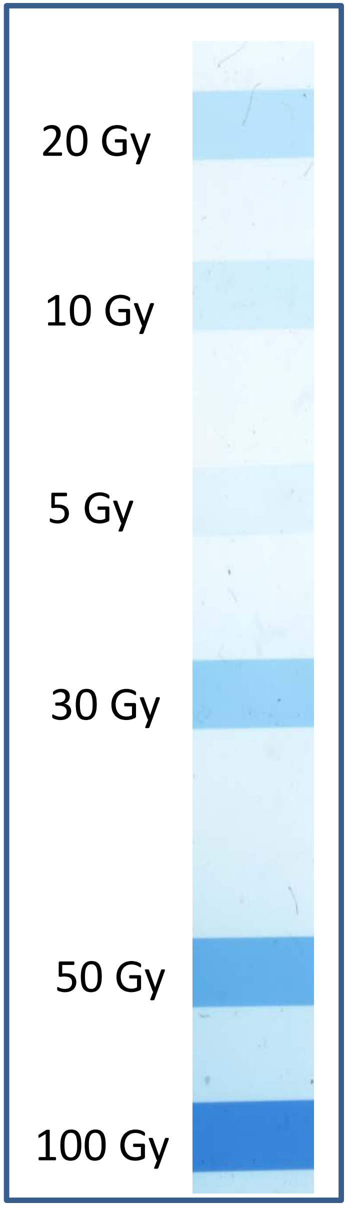


Ionization chamber for operative dosimetry control



Basic characteristics	
Data acquisitions frequency	2.5-7500 Hz
The accuracy of the conversion factor	1%
Range of ADC	22 bit
1 bit of ADC	1 nA/V or 1 µA/V

GAFCHROMIC® HD-810 Radiochromic Dosimetry Film



20 Gy

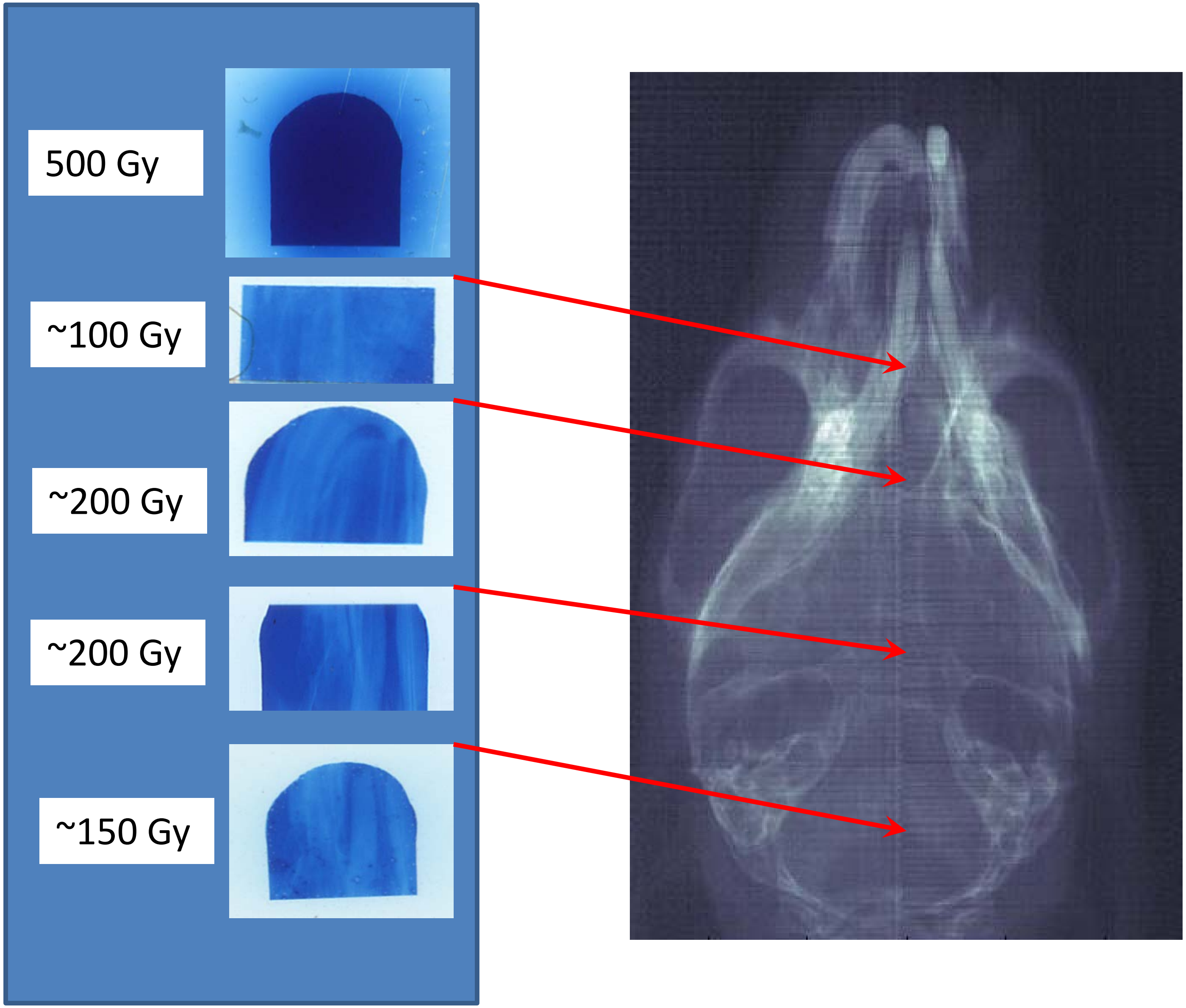
10 Gy

5 Gy

30 Gy

50 Gy

100 Gy



500 Gy

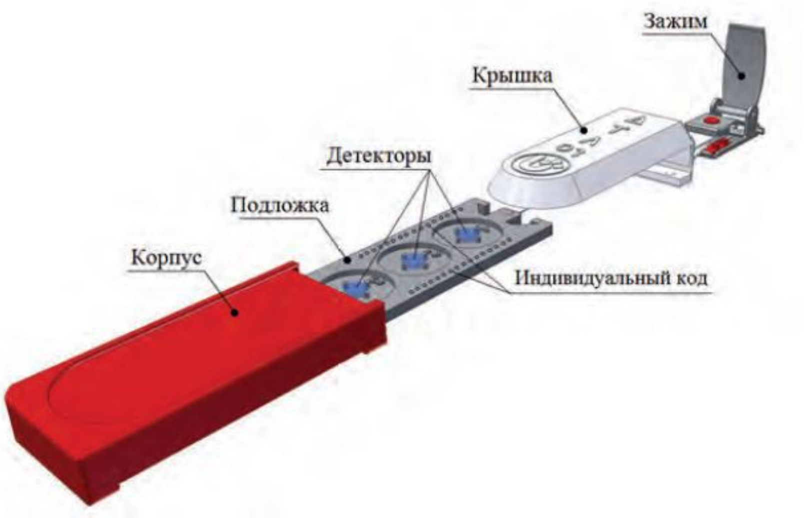
~100 Gy

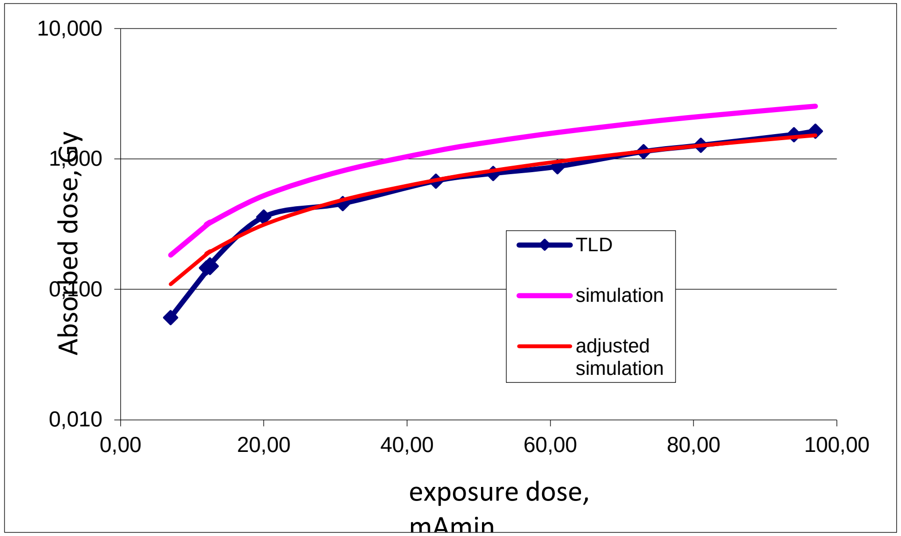
~200 Gy

~200 Gy

~150 Gy

Thermoluminescent dosimeters based on LiF crystals

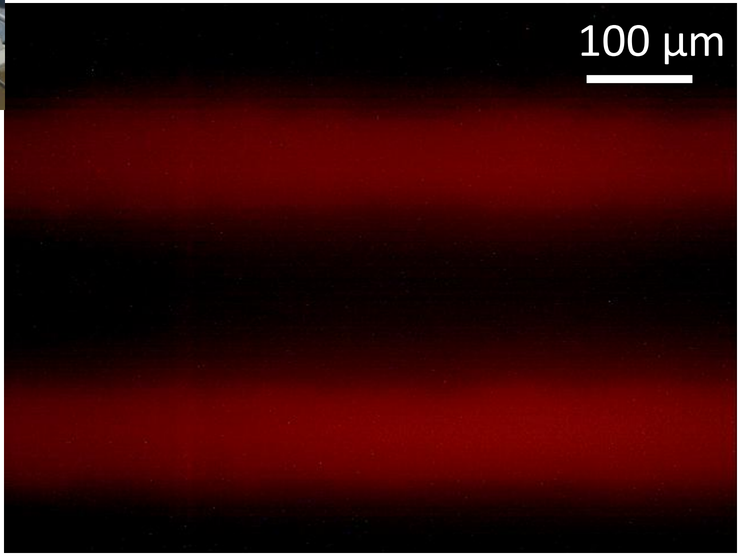




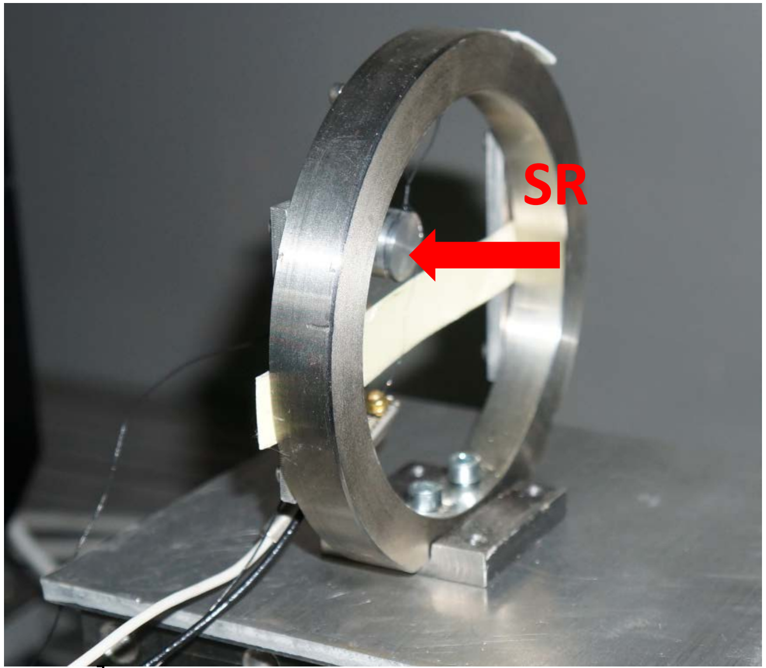
Thermoluminescent dosimeters based on LiF crystals

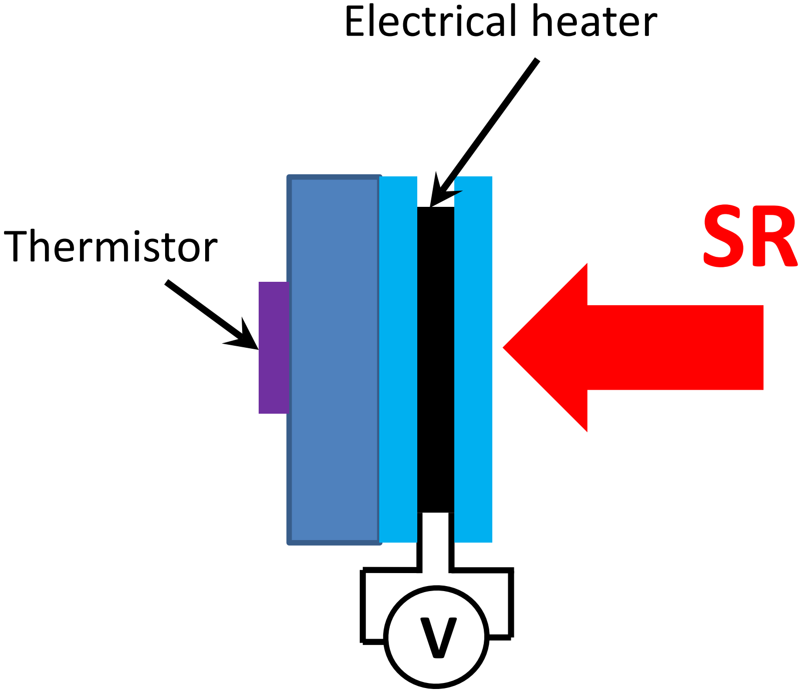
Reader luminescence irradiated LiF crystals with 5 µm spatial resolution

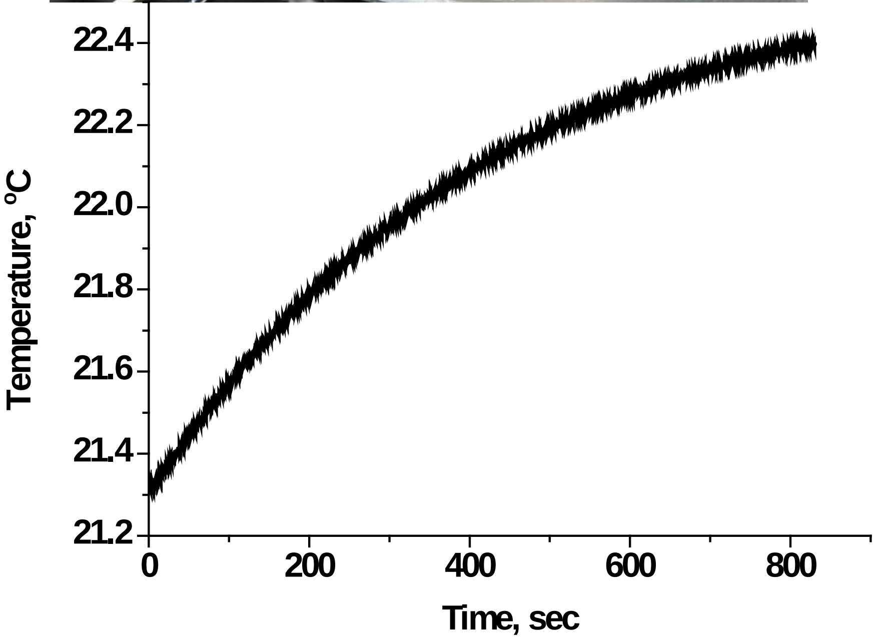
Luminescence of irradiated LiF crystal by dose 4 Gy



Tantalum calorimeter



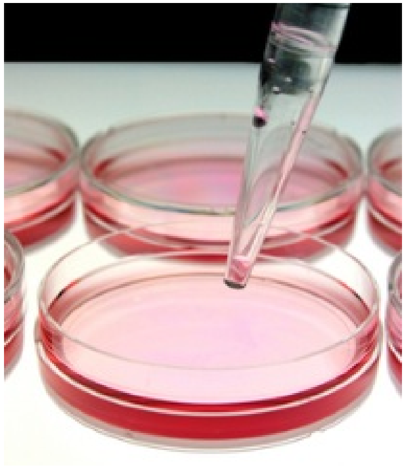




We measure the absolute dose rate of the filtered beams with a tantalum calorimeter.

In our experiments we have two base directions:

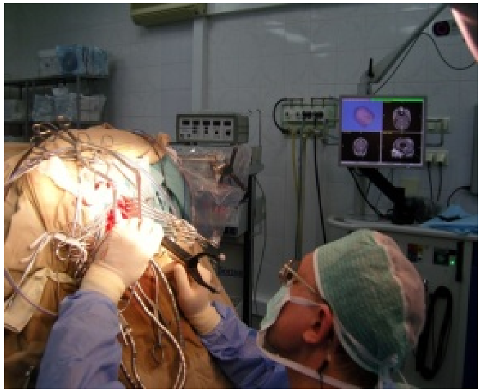
1 . In-vitro experiments on human glioma cell line



2. In-vivo experiments on Hairless SCID (Severe combined immunodeficiency) mouse

In-vitro experiments

We used human glioblastoma cell line U-87, obtained from American Type Culture Collection (ATCC)



clinic

Primary Culture U-87

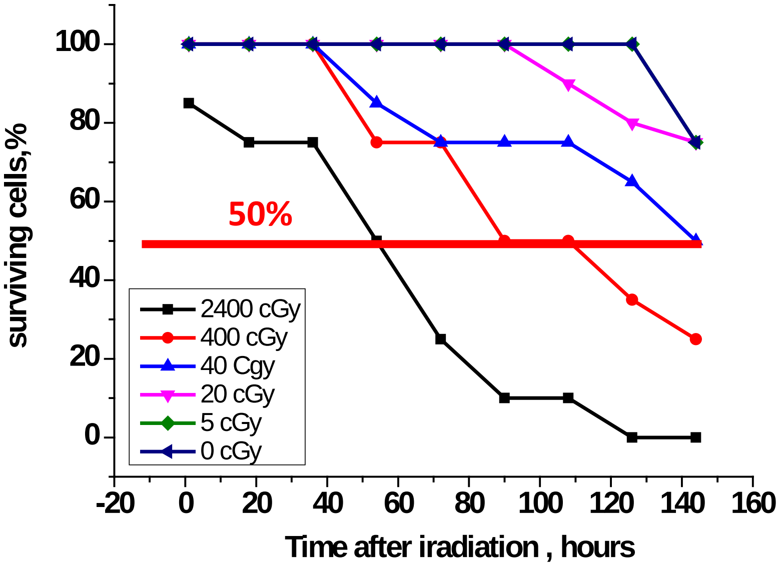
Cryobank
SPF-Vivarium

In-vitro
experiments

Determination of the lethal dose (LD_{50}) for glioma cell U-87

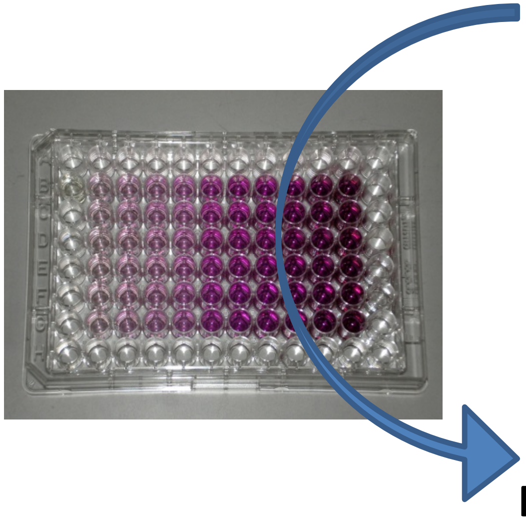
MTT -TEST

A yellow Tetrazole, is reduced to purple Formazan in living cells.



Yellow Tetrazole

3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide



Mitochondrial Reductase

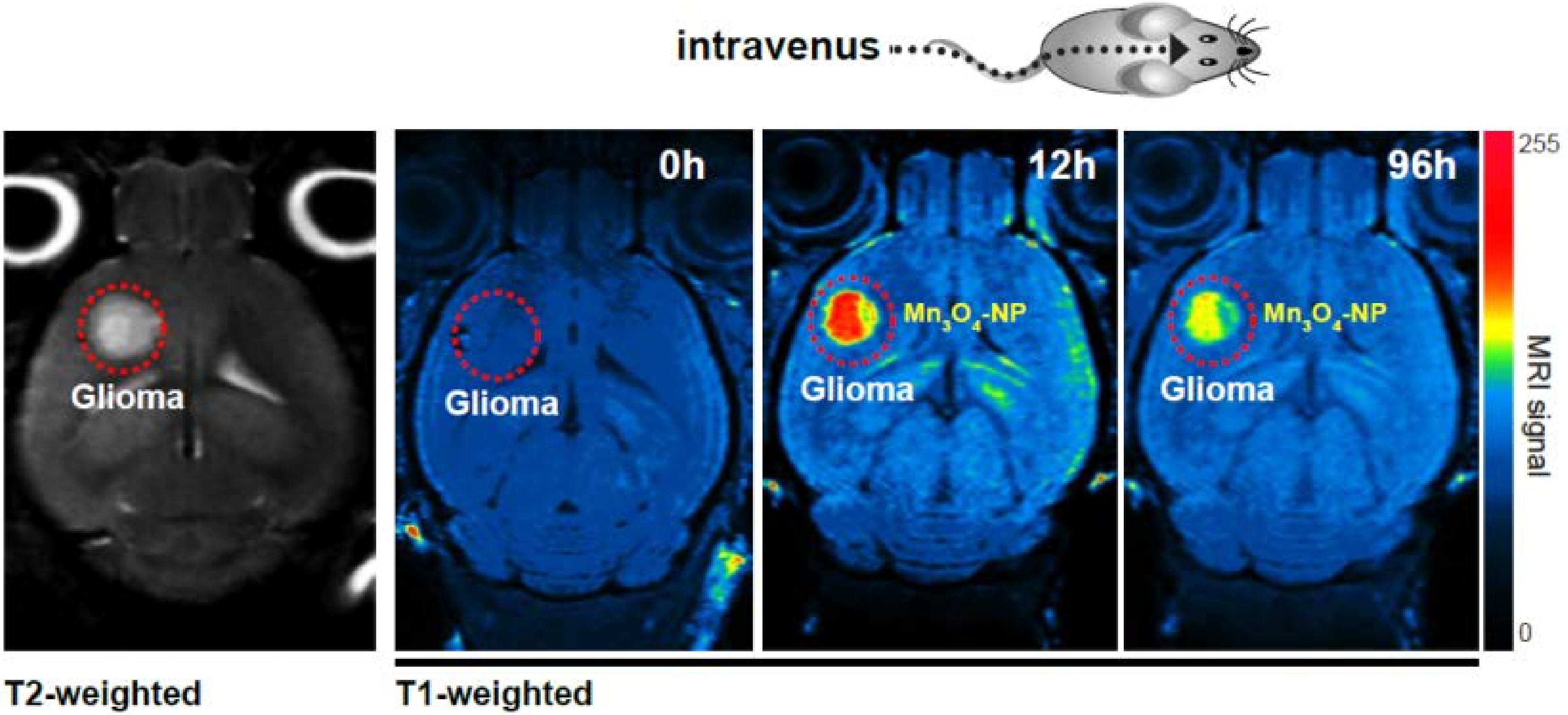
Formazan

(E,Z)-55(3-(4,5-dimethylthiazol-2-yl)-1,3-diphenyltetrazolium bromide

+

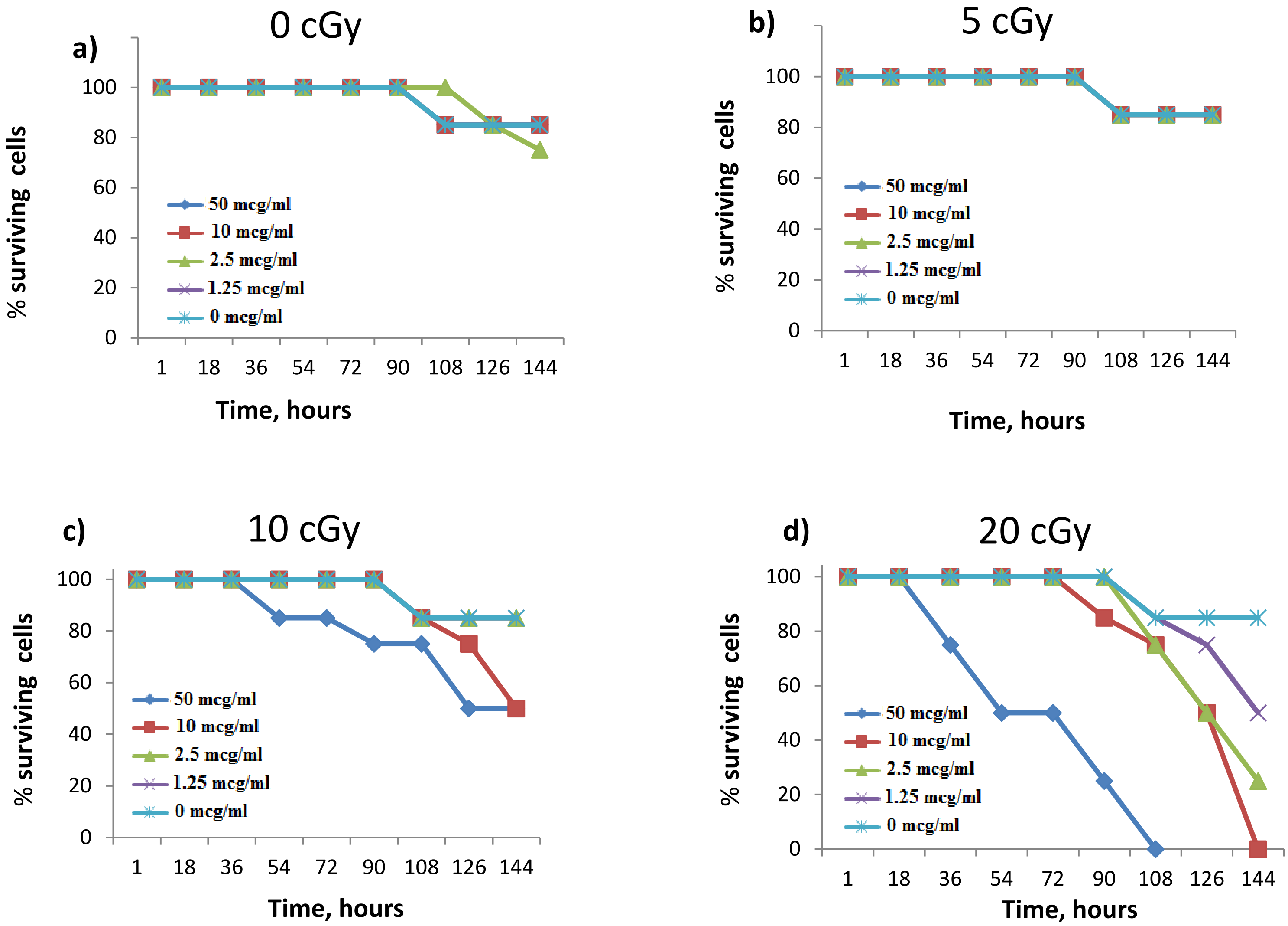
Colour

Application of manganese oxide nanoparticles to enhance the effect microbeam radiation therapy

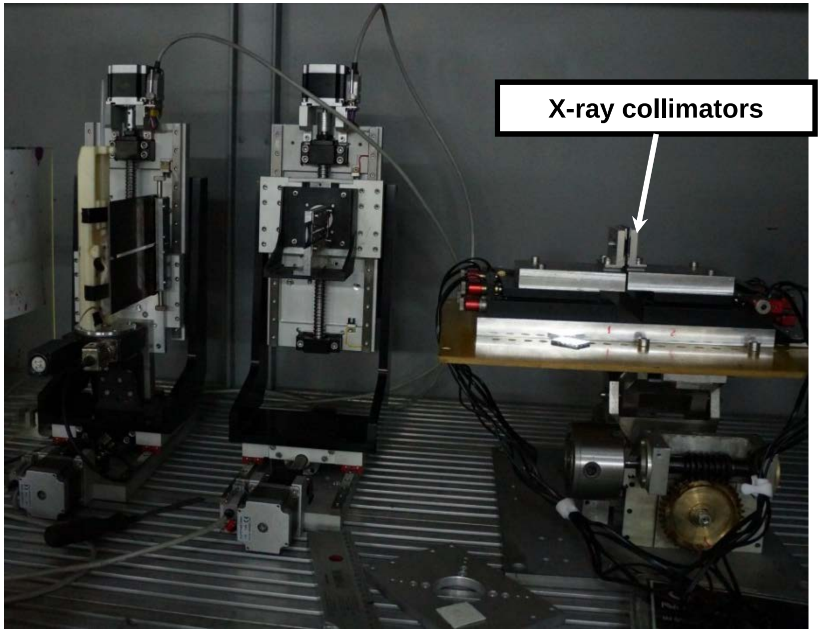


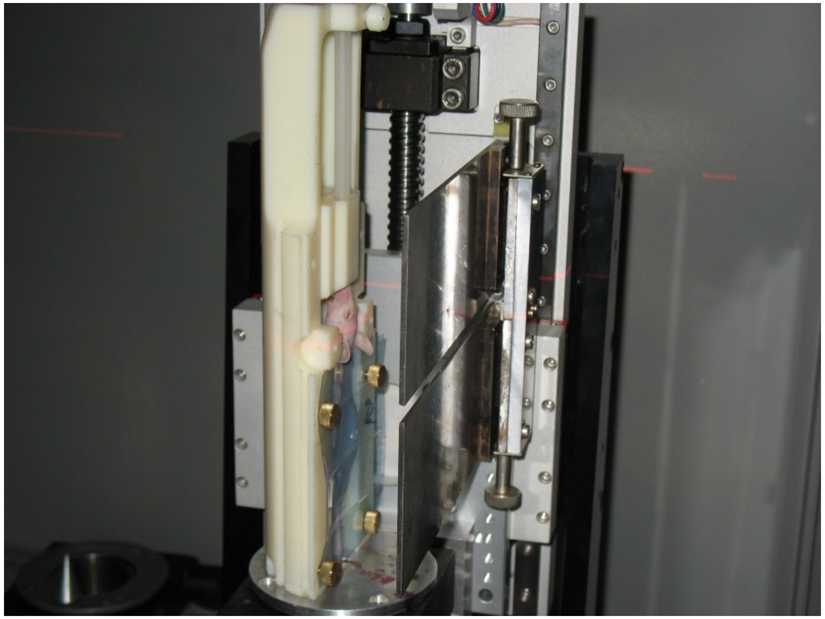
In our work we try to offer new possibilities for improving therapeutic technologies based microbeam radiation which is consists in combined use of radiotherapy and applying nanoparticles. In our experiments we used of combination of the effect of radiotherapy with saturation of tumor cell with nanoparticles of manganese oxide. This combination provide a synergistic effect for cytolysis of glioma cell based on nanoparticles enhance oxidative effect of reactive oxygen.

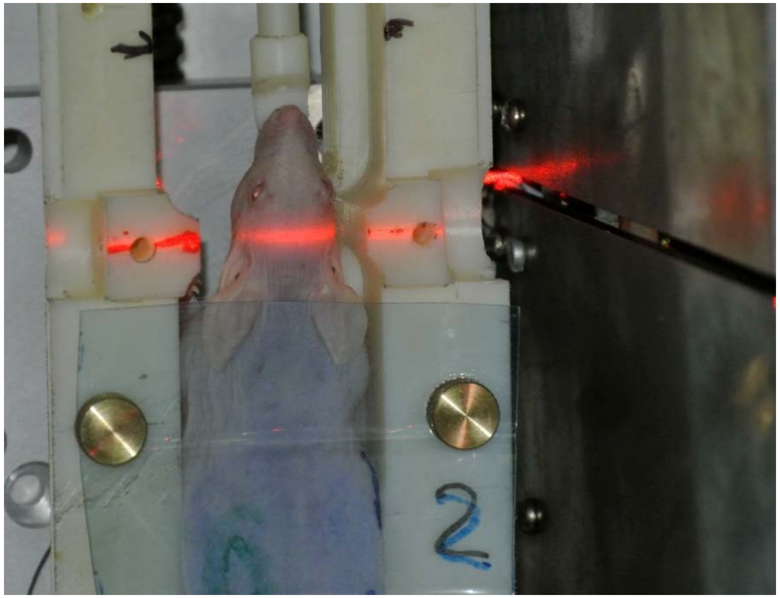
Cytopathic effects for different irradiation doses of glioma cells U87 depended on incubated concentration of manganese oxide nanoparticles



In-vivo experiments on Hairless SCID mouse





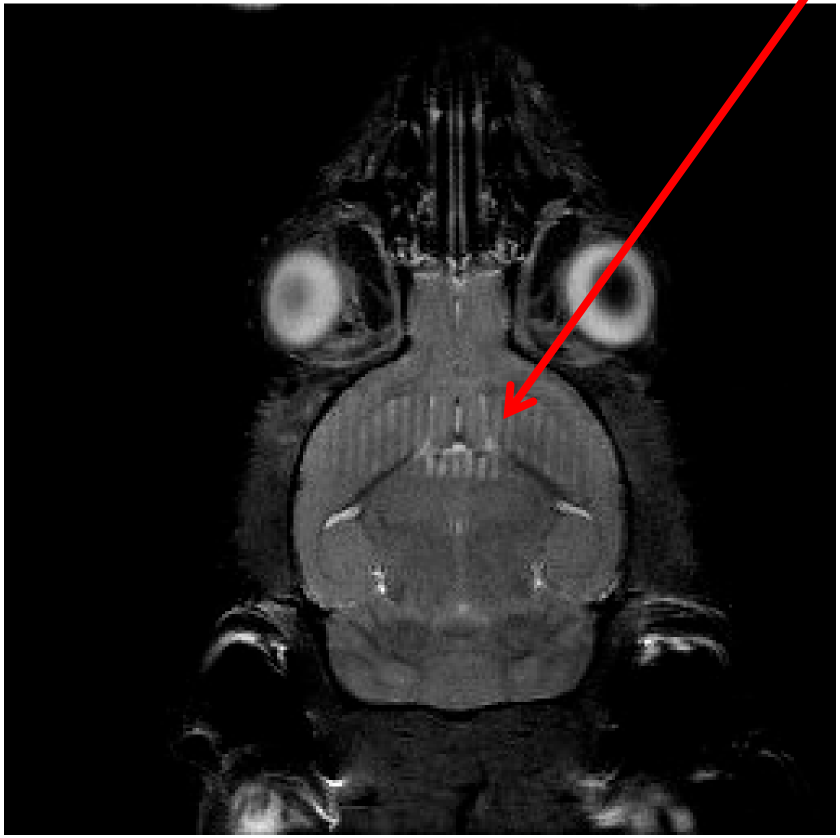


In-vivo experiments on Hairless SCID mouse

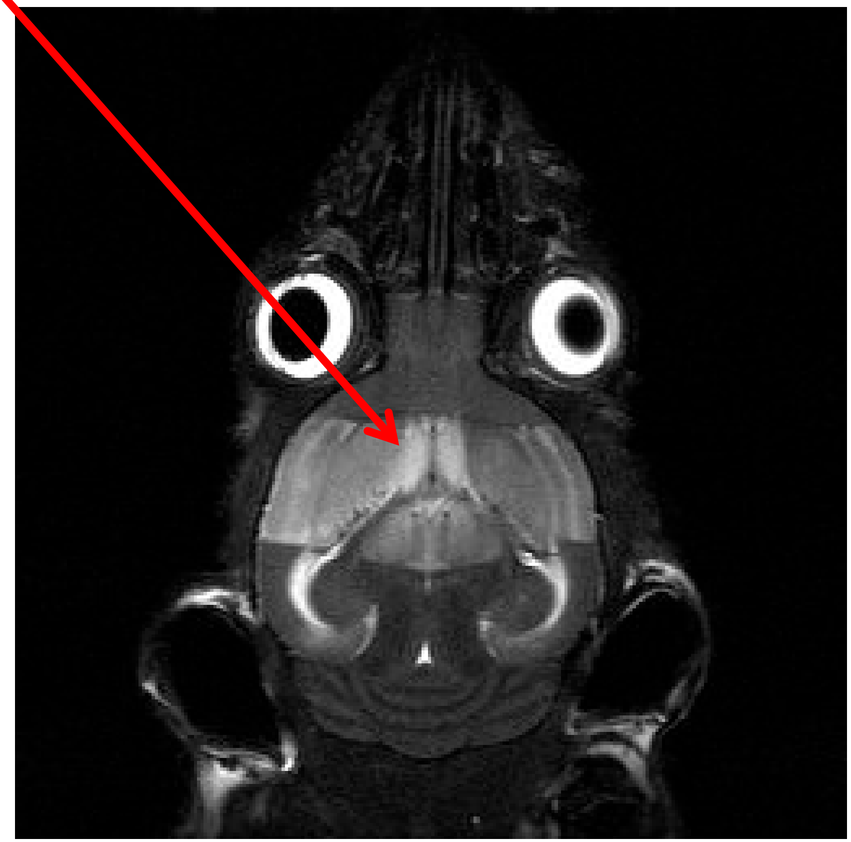
In postirradiation period the animals was monitored on the NMR tomograph Bruker «BioSpec 117 / 16USR»
At present time this one is the most powerful (11.7 T) NMR tomograph in Russian Federatin to study the morphological and functional characteristics of mice.

In-vivo experiments on Hairless SCID mouse

Irradiations zone

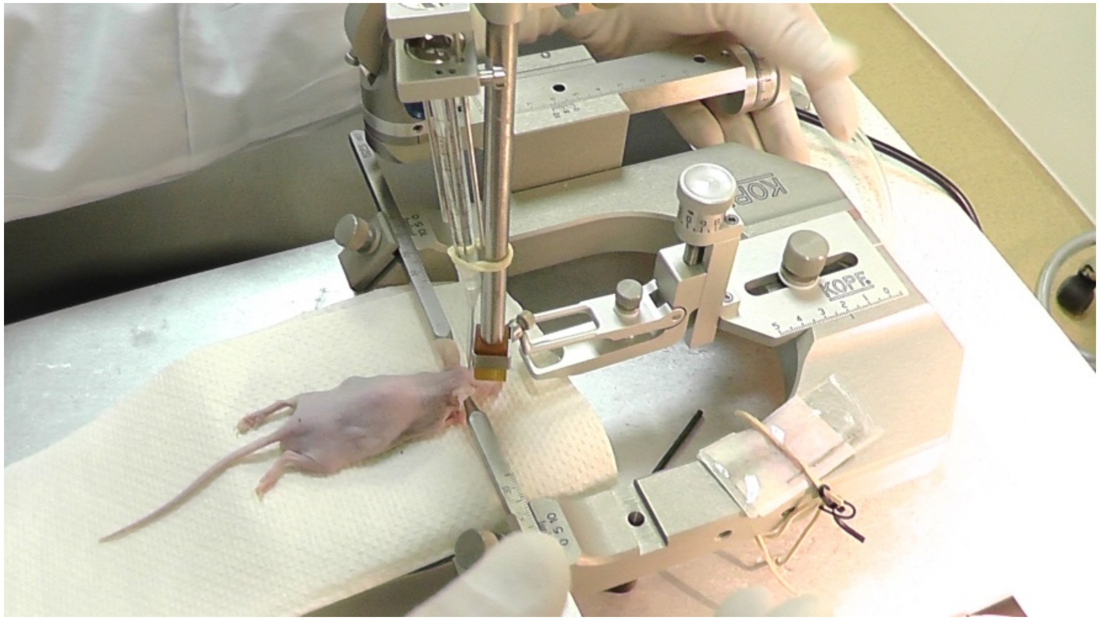


Microbeam irradiation
800 Gy
(mouse survived)



Broad beam irradiation
400 Gy
(mouse died at next day)

In-vivo experiments on Hairless SCID mouse



In the last week we carried out experiments with microbeam on mice with implanted glioma tumors. Irradiation dose was from 400 to 1000 Gy.

The animals were injected intracerebrally once $5*10^5$ cells (5 µl suspension) of human glioma cells.

Thank you very much for your attention !