Effectiveness of the proton therapy delivered at JINR and plans for wide application in cooperation with other international centers

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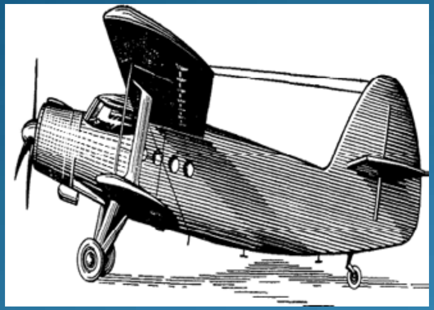
110th session of the Scientific Council

Road Map for the development of hadron therapy and associated nuclear medicine methods at JINR:



Development of 3D conformal Proton therapy

Design of various devices for proton therapy

Validation of the proton therapy method

Application of 3D conformal therapy

Construction of equipment for medical centers

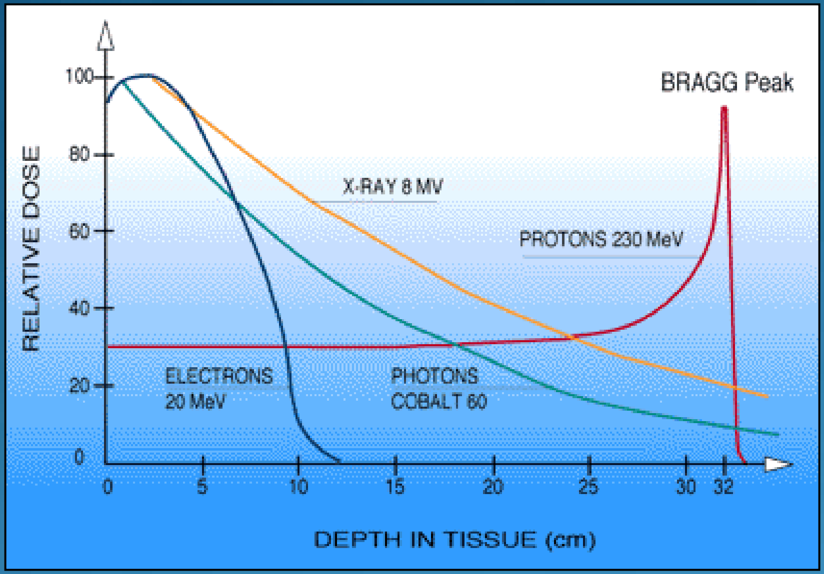
Education of personnel for PT centers

Invention of SC machines for Proton and Carbon Therapy

Development of new methods and devices

Design and construction of medical centers

HADRON THERAPY IN THE WORLD AND IN RUSSIA



There are 25 centers of the proton therapy and 4 centers of carbon therapy in the world now.

In total more than 60 thousand patients were treated by hadron therapy method

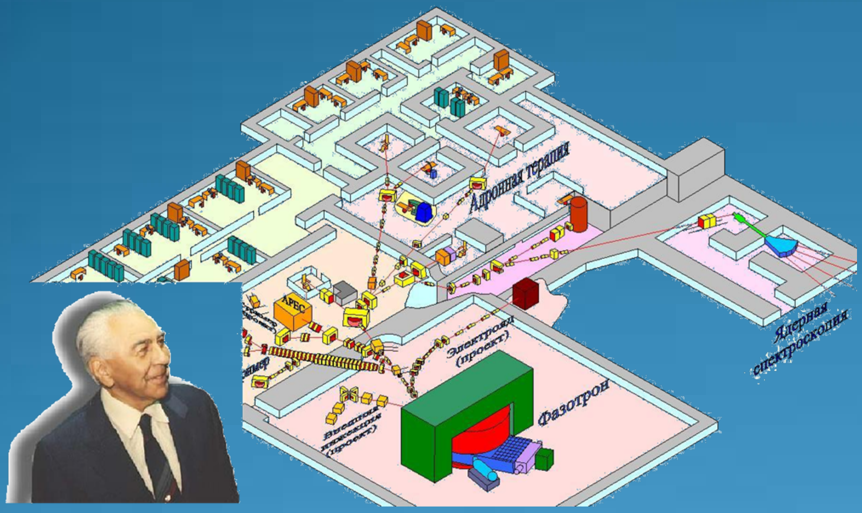
At present 90% of patients are treated now by the hospital based facilities.

Total number of tumor patients in Russia is about 2.3 million,

about 450 thousand of new patients appear in Russia every year,

out of them the proton therapy is recommended to 50 thousand

JINR Medical-Technical Complex at DLNP Phasotron



1967 – First investigations of cancer treatment;

1968 –1974 –84 patients were irradiated by proton beams on synchrocyclotron;

1975 –1986 – Upgrade of synchrocyclotron, creation of Medic-Technical Complex (MTC) of hadron therapy in JINR;

1987– 1996 –40 patients were irradiated by proton beams;

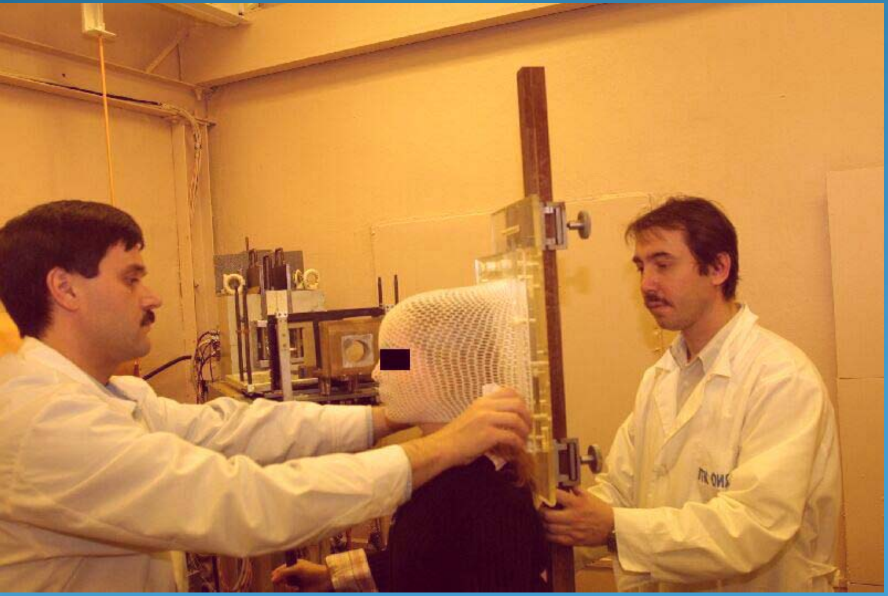
1999, – Creation of radiological department in Dubna hospital;

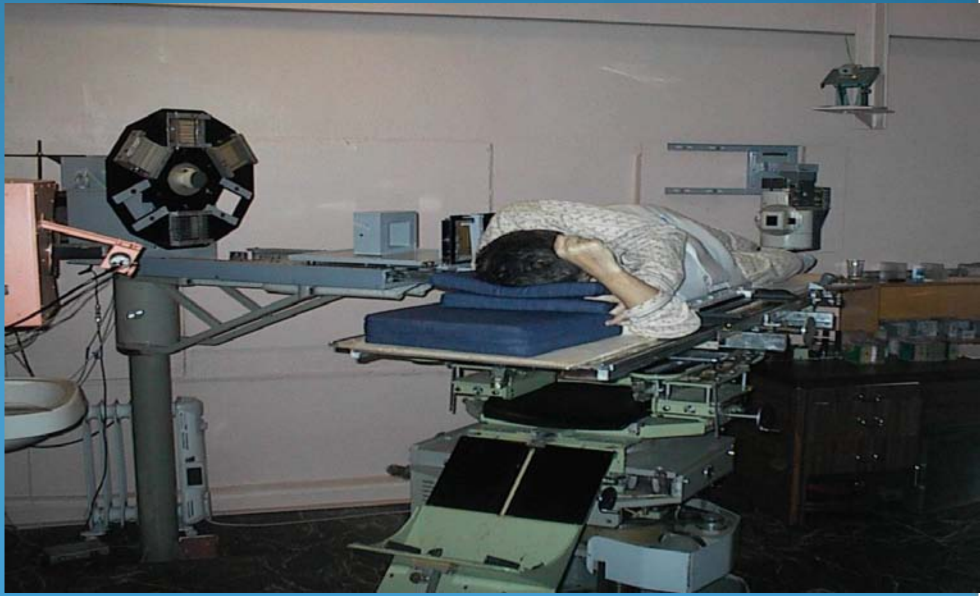
1999 – 2011, – 780 patients were irradiated by proton beam.

The work is performed as a research in Collaboration with Medical Radiological Research Center of Russian Medical Academy of Science (Obninsk).

JINR MTC WITH PROTON BEAMS

3D conformal proton beam treatment was realized in Russia only at JINR.

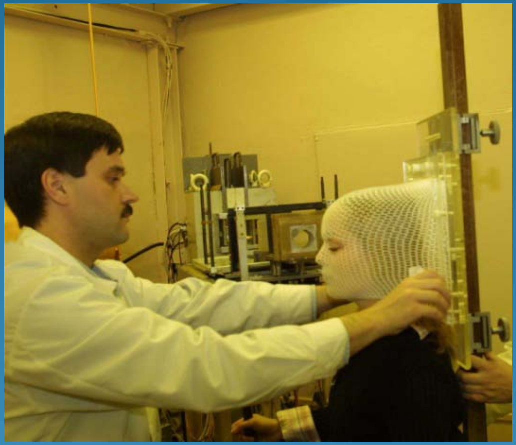


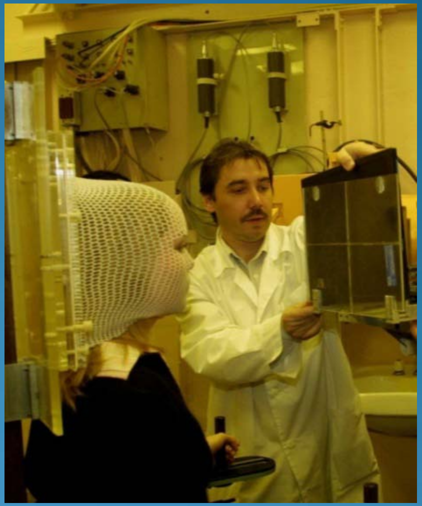


Cancer treatment in cabin №1

Prostate treatment equipment

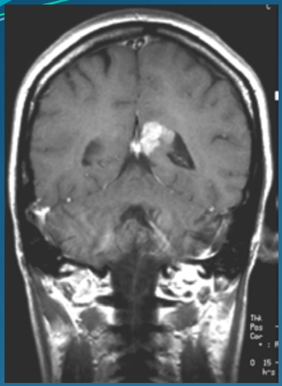
Procedure for Treatment



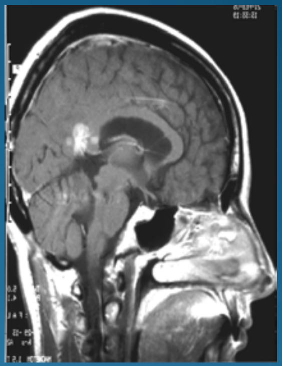


1. Diagnostic imaging
2. Planning
3. Individual manufacturing
4. Immobilization
5. Verification
6. Irradiation
7. Follow up

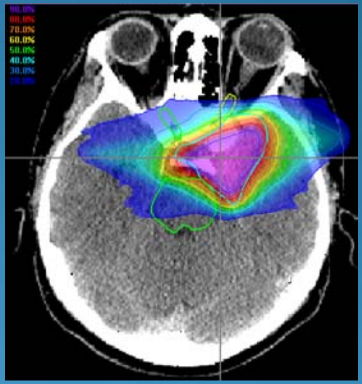
Step by step (I)

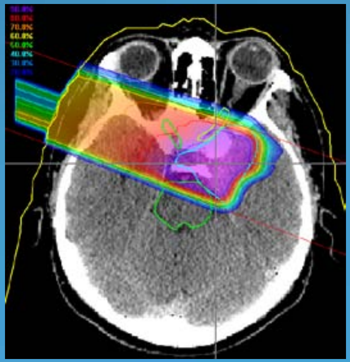


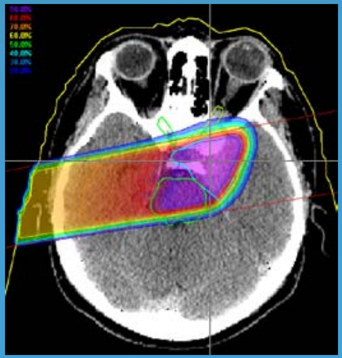
Computer and Magnetic Resonance Imaging are used for diagnostics and preparation

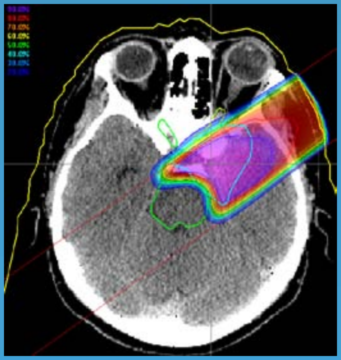


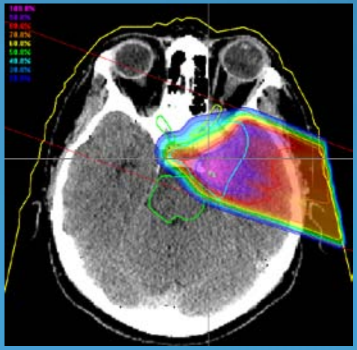
The modern 3D Treatment Planning System (TPS) from LLUMC is used. This system was adjusted for the use with Dubna beam and calibrated in several dosimeter experiments, where the algorithm was checked. Good agreement of calculated and measured dose distributions was achieved. Treatment plan is also x-checked by the local TPS.





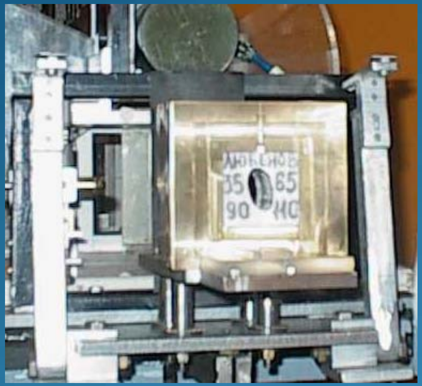


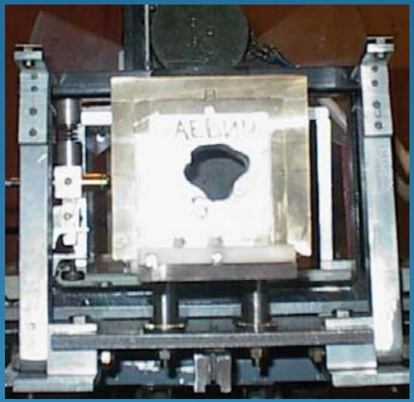


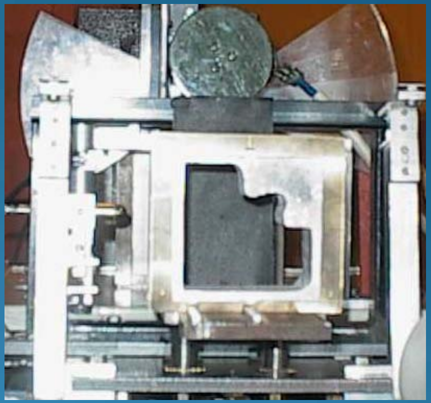


Step by step (II)

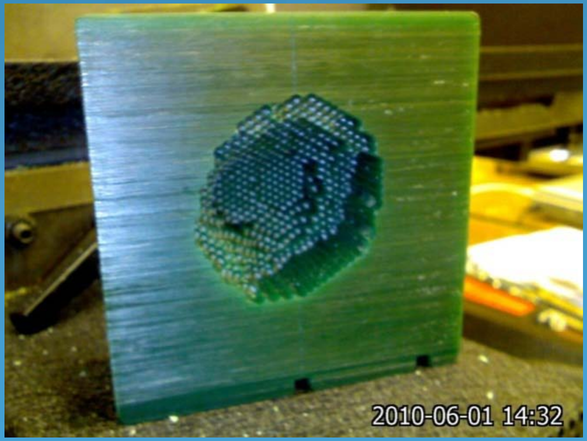
For each proton beam individual complex shape apertures are manufacturing





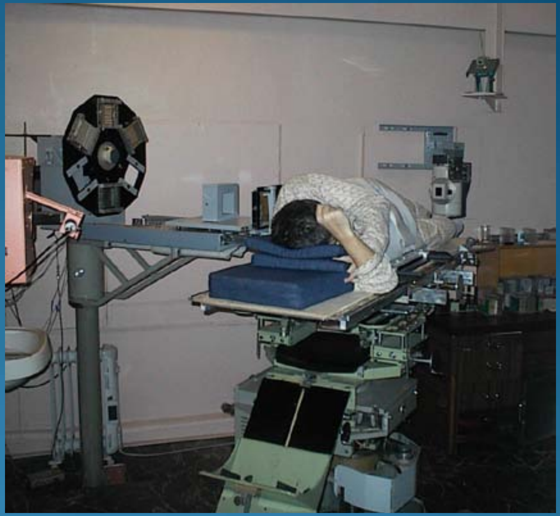


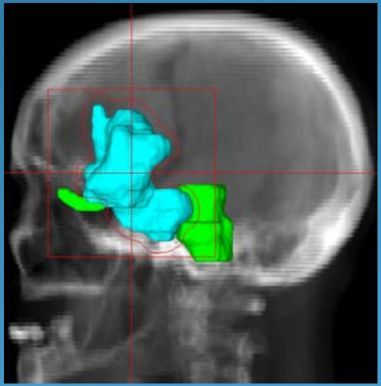
Bolus-compensators at present time are made by digital milling machine



Step by step (III)

Immobilization devices

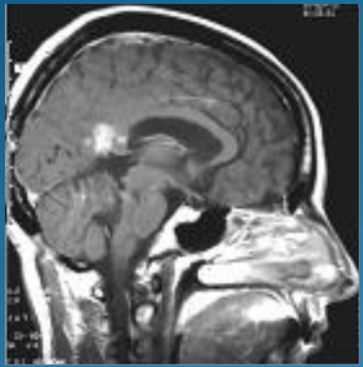


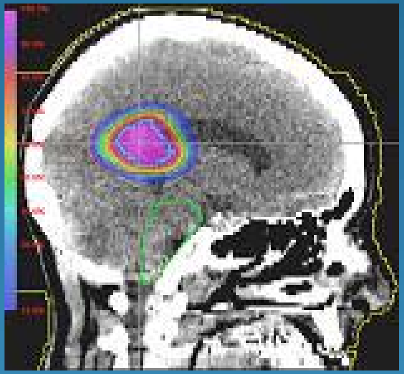


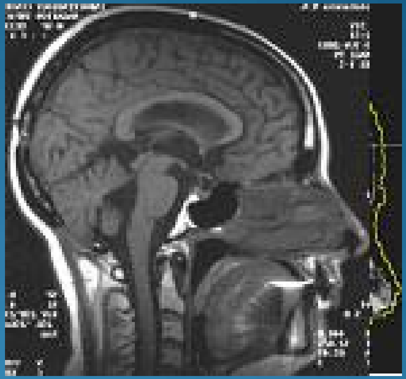
Final stage in preparation is simultaneous X-ray image with bones structure, low intensity proton beam and digital reconstruction of the coordinate axes, target and critical structures

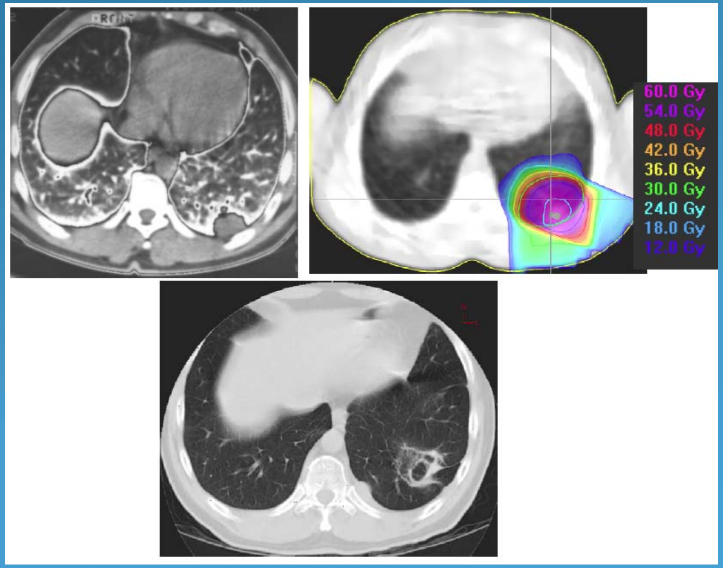
Examples

Brain cancer – before (left), plan and 3 months after (right) treatment









Proton radiation therapy (60 GyE in 10 fractions) of the renal cell carcinoma metastasis to the left lung:
Top Left **– before treatment;**
Top Right **– Treatment plan;**
Bottom **– 8 months after treatment.**
Radiation pneumonitis transformed to localized fibrosis with no clinical symptoms. Tumor disappeared completely.

Treatment at JINR

	No of accelerator runs	No of patients treated
1999	*2*	*3*
2000	*4*	*36*
2001	*5*	*49*
2002	*4*	*34*
2003	*6*	*84*
2004	*6*	*90*
2005	*1*	*24*
2006	*Fire accident*	*----*
2007	*7*	*84*
2008	*6*	*87*
2009	*7*	*106*
2010	7	122
2011.08	4	61

Diseases treated

Meningiomas – 130 pts
Chordomas, chordosarkomas – 27 pts
Gliomas – 48 pts
Acoustic Neurinomas – 9 pts
Astrocytomas – 33
Paragangliomas – 5 pts
Pituitary Adenomas – 22 pts
AVMs – 63 pts
Brain and other metastasis – 59 pts
Other head and neck tumours – 194 pts
Melanomas – 11 pts
Skin diseases – 45 pts
Carcinoma metastasis of the lung – 9 pts
Breast cancer – 46 pts
Prostate Adenomas – 1 pt
Sarcomas – 14 pts
Other – 28 pts

Number patients treated in 1999-2011 is 780
The geography includes Russia and JINR Member States

World statistics

Patient Statistics (for the facilities in operation end of 2010):

WHERE		WHAT	FIRST PATIENT	PATIENT TOTAL	DATE OF TOTAL	
Canada	Vancouver (TRIUMF)	p	1995	152	Dec-10	ocular tumors only
China	Wanjie (WPTC)	p	2004	1078	Dec-10	
China	Lanzhou	C ion	2009	126	Dec-10	
England	Clatterbridge	p	1989	2021	Dec-10	ocular tumors only
France	Nice (CAL)	p	1991	4209	Dec-10	ocular tumors only
France	Orsay (CPO)	p	1991	5216	Dec-10	4245 ocular tumors
Germany	Berlin (HMI)	p	1998	1660	Dec-10	ocular tumors only
Germany	Munich (RPTC)	p	2009	446	Dec-10	
Germany	HIT, Heidelberg	C ion	2010	400	Dec-10	estimate; has to be confirmed
Germany	HIT, Heidelberg	p	2010	40	Dec-10	estimate; has to be confirmed
Italy	Catania (INFN-LNS)	p	2002	174	Mar-09	ocular tumors only
Japan	Chiba (HIMAC)	C ion	1994	5497	Aug-10	
Japan	Kashiwa (NCC)	p	1998	772	Dec-10	
Japan	Hyogo (HIBMC)	p	2001	2382	Nov-09	
Japan	Hyogo (HIBMC)	C ion	2002	638	Nov-09	
Japan	Tsukuba (PMRC, 2)	p	2001	1849	Dec-10	
Japan	Shizuoka	p	2003	986	Dec-10	
Korea	Ilsan, Korea	p	2007	648	Dec-10	
Russia	Moscow (ITEP)	p	1969	4246	Dec-10	
Russia	St. Petersburg	p	1975	1362	Dec-10	
Russia	Dubna (JINR, 2)	p	1999	720	Dec-10	
South Africa	iThemba LABS	p	1993	511	Dec-09	
Sweden	Uppsala (2)	p	1989	1000	Dec-10	
Switzerland	Villigen PSI, incl OPTIS2	p	1996	772	Dec-10	47 ocular tumors
CA., USA	UCSF - CNL	p	1994	1285	Dec-10	ocular tumors only
CA., USA	Loma Linda (LLUMC)	p	1990	15000	Jan-11	
IN., USA	Bloomington (MPRI, 2)	p	2004	1145	Dec-10	
MA., USA	Boston (NPTC)	p	2001	4967	Dec-10	
TX, USA	Houston	p	2006	2700	Dec-10	about 500 with scanning
FL, USA	Jacksonville	p	2006	2679	Dec-10	
OK, USA	Oklahoma City (ProCure PTC)	p	2009	21	Dec-09	
IL, USA	CDH Warrenville	p	2010		Oct-10	
				64702	**Total**	
			thereof	6661	C-ions	
				58041	protons	

Dubna results on AVM and other deseases

- ✓ Arterio Venous Malformations - ~ 95% complete or partial obliteration

PTCOG 50 May 2011

Proton radiosurgery of intracranial arteriovenous malformation

Intracranial **AVM** had been treated in **61** patients since December 2001 till December 2010. Range of volume of treated AVM was 1 to 82 cc: 1 -5 cc - in 13 patients, 5-25 cc- in 36, > 25 cc- in 12. We accepted international protocol for dosimetry planning and absorbed dose selection, developed primarily at The Loma Linda-University Medical Center by Dr Shulte and Dr Levy. Isocenter dose: for non-eloquent small- and medium size AVM - 25 GyE; for eloquent small and medium size AVM - 24 GyE; for large AVM - 20-23 GyE. Doses were delivered in two consecutive days fractions. Target volume included 70-90% isodose line - 17,5-22.5 GyE.

Follow-up consisted in MRI scans every 6 months and cerebral angiography 3 years after radiosurgery treatment. 55 patients have got observation period more than 24 months; from them 3 died (2 from intercurrent diseases, 1 from AVM hemorrhage during latency period), 6 were lost for contact for unknown reasons. Consequently, 46 patients were available for analysis. Complete obliteration was confirmed in 19 patients (41,3%), partial obliteration-in 25 (54,35%), from them 44%- were 80-99% obliteration. Two patients (4,35%) had no effect.

- ✓ Meningiomas - Dubna preliminary analysis gives ~80% compared to the world result – 93% and 77% (for 5 and 10 years)

Other forms are not yet statistically conclusive for publication but Dubna results are consistent with the world statistics of :

- ✓ Gliomas – 43% and 97% (18months)
- ✓ Chordomas – 60% (no recidive)
- ✓ Pituitary Adenomas – 70-90% (for micro-adenomas)

http://mtk.jinr.ru

Development of collaboration with INR (Troitsk) related to 3D conformal proton therapy

INR proton therapy treatment room

Medical treatment room for conventional radio-therapy on the basis of linear accelerator

Development of JINR-INR collaboration

Exchange of experts and information about PT technology and TPS

Development of diagnostic and verification methods

Participation in common projects

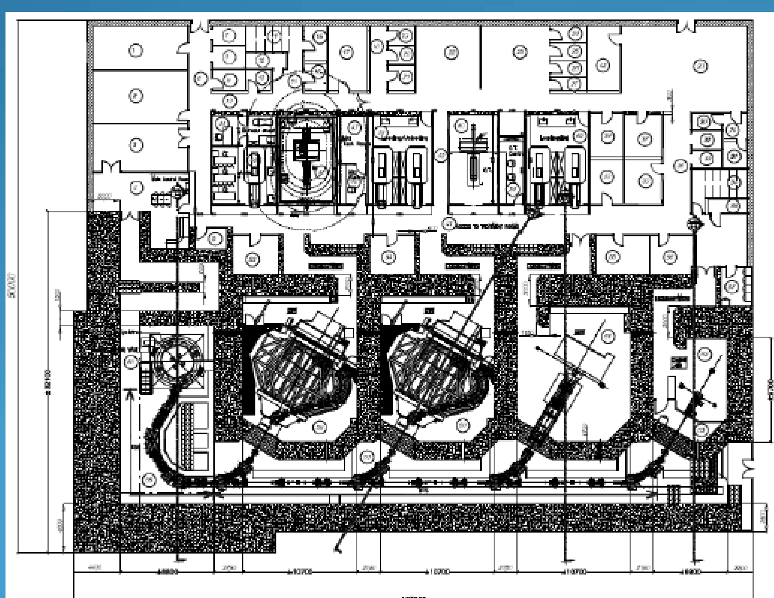
Proton Therapy technology transfer to the specialized medical centers

Project of
Radiation Medicine Center

Administration of Dubna and Moscow region

Rosnano Corporation
Project ID 1143

Moscow Oncological Center and Academy of Medical Sciences

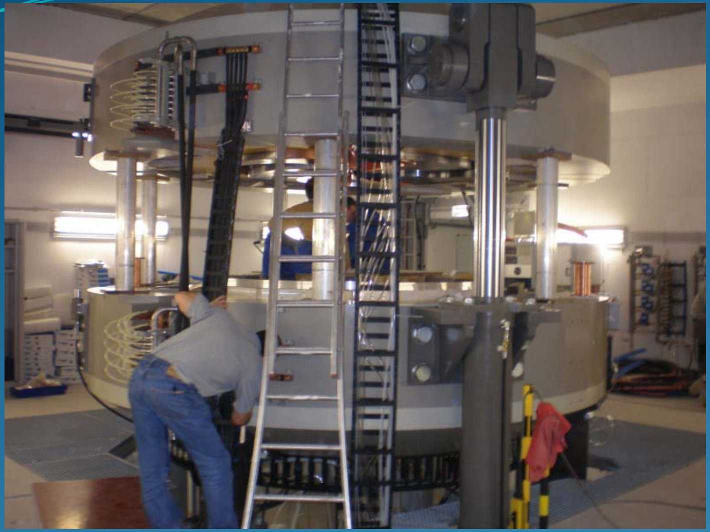


Manifold task: accelerator and beam transport are necessary but not sufficient parts.

Very complex are: medical support, certification of method and licensing of equipment, software validation and approval of the whole procedure.

Possible solution – Collaboration with world known experts of Proton Therapy.

Collaboration of JINR and Ion Beam Applications (IBA, Belgium)



Beam dynamic and magnetic field simulation performed by JINR experts for IBA medical cyclotron C235:

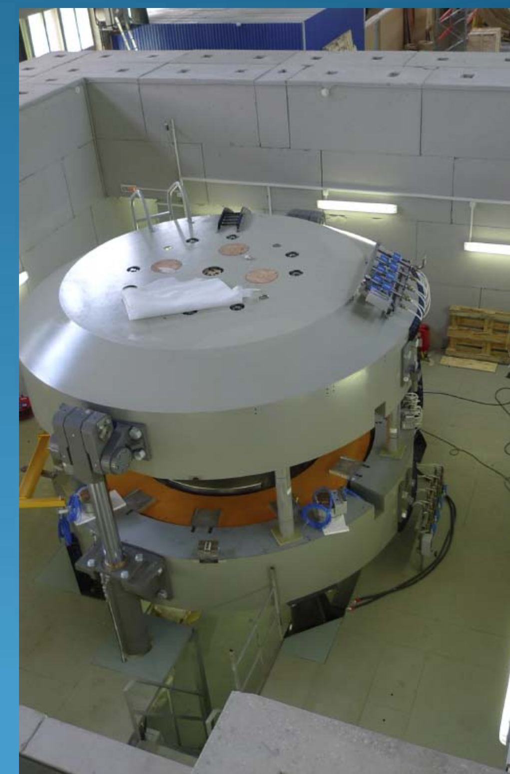
Parameter	C235	C235-V3
Optimization of magnetic field at modification of sector		Modification of azimuthal angle of sectors on $1{,}5^0$-2^0 at R>80
Vertical betatron frequency is increased at R>80	Q_z=0,25	Q_z=0,45
Vertical coherent beam displacement related to effects of median plate should be reduced	6-7mm	1,5-2mm
Beam losses should be reduced at proton acceleration	50%	15%
Beam losses at extraction were reduced	50%	25%
Reduction of radiation dose of cyclotron elements caused by of beam current losses		Radiation dose of cyclotron elements should be reduced several times

Modifications in the design were accepted by IBA and an agreement was reached to construct such cyclotron at JINR.

This cyclotron will be used for pilot Russian Nuclear Medicine center, which is constructed by Federal Medico-Biological Agency.

***Special engineering center was created at JINR in 2008-2010 for testing of medical accelerator equipment*.**

June 2011, delivery of cyclotron magnet



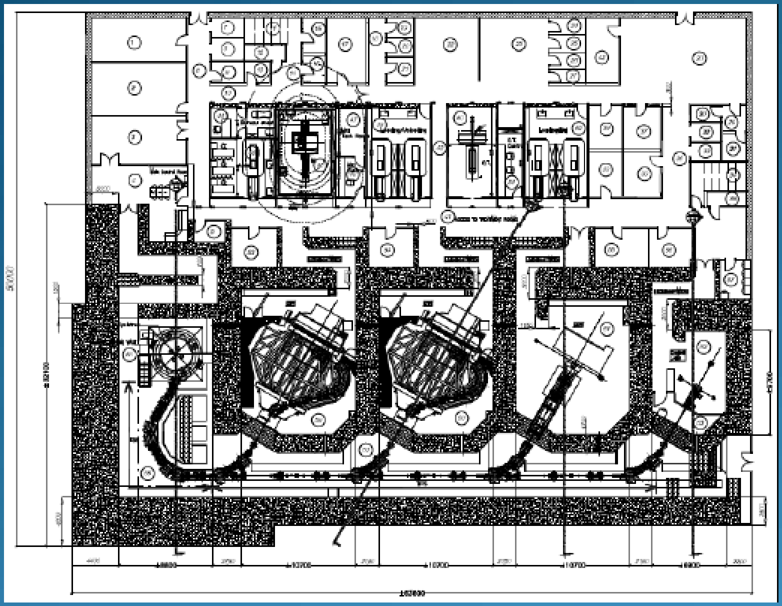
August 2011, ready for magnetic field tuning

Assembling and first magnetic tests of cyclotron C235 V3 at JINR

Dimitrovgrad project

Certification of PT equipment was done for the first time in Russia

(the only one yet)



- ✓ ***Design***
- ✓ ***Construction***
- ✓ ***Installation***
- ✓ ***Service***

Education of personnel for Dimitrovgrad center at JINR:

✓ ***Local team (~6 persons) for equipment service coming to Dubna for one year training (in collaboration with IBA)***

✓ ***Training of students prepared for Dimitrovgrad by MEPhI (in collaboration of MEPhI with JINR UNC and Laboratories)***

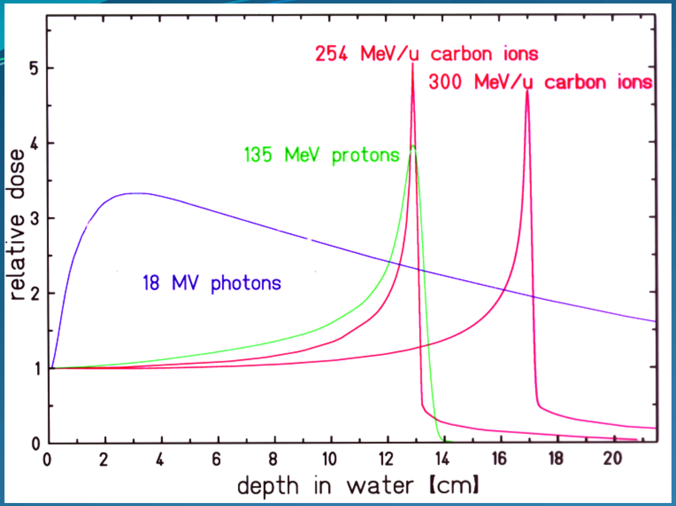
Possible projects in Russia

- ❑**Dimitrovgrad**
- ❑**Obninsk**
- ❑**Tomsk**
- ❑**Yekaterinburg**

and JINR Member States

- ❑**Kazakhstan**
- ❑**Ukraine**
- ❑**Vietnam**
- ❑**Poland**

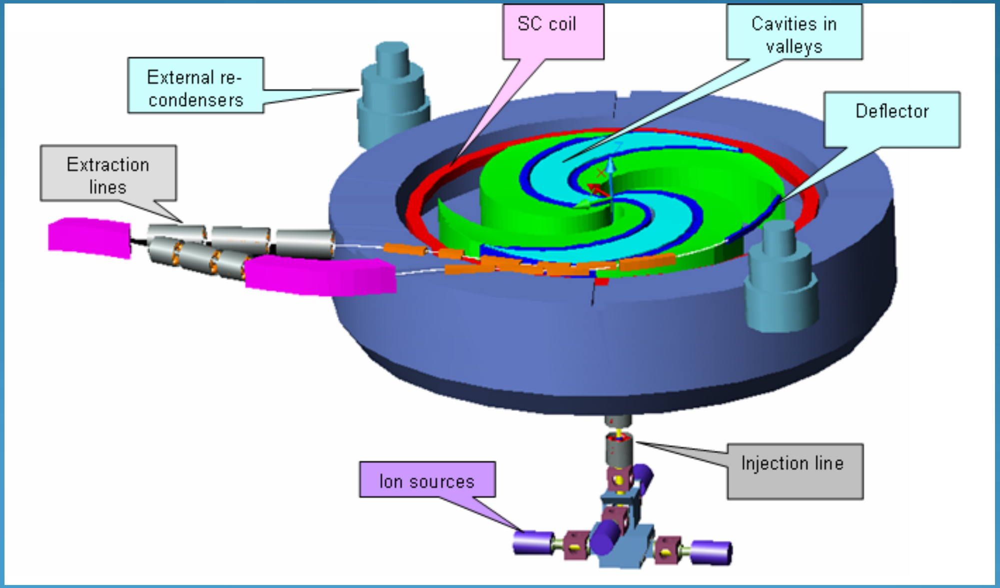
Cancer Treatment with Carbon beam



The carbon $^{12}C^{6+}$ ion beams at intensity of 10^9 pps are efficiently used for cancer treatment especially for patients with radioresistant tumor targets.

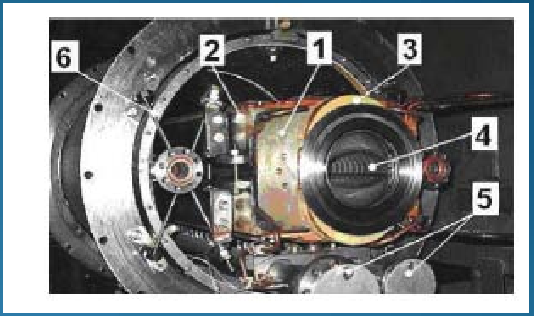
In collaboration with IBA the JINR team has designed the C400 – Compact Super Conducting Cyclotron for Hadron Therapy

accelerated particles	**H_2^+, $^4He^{2+}$, ($^6Li^{3+}$), ($^{10}B^{5+}$), $^{12}C^{6+}$**
final energy of ions, protons	**400 MeV/amu 265 MeV**
extraction efficiency	**~70 % (by deflector)**
number of turns	**~1700**
total weight	**700 tons**
outer diameter	**6.6 m**
height	**3.4 m**
pole radius	**1.87 m**
hill field	**4.5 T**
valley field	**2.45 T**
RF frequency	**75 MHz**



The construction of C400 has started in September 2010 in the framework of Archade project (France, Caen)

Nuclotron technologies as a basis of superconducting medical synchrotron for hadron therapy

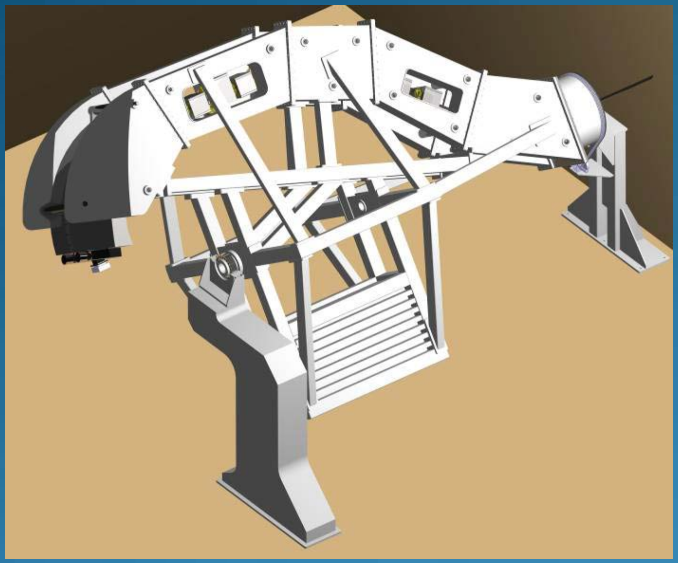


One of the possible magnetic structures and parameters of SC synchrotron

Number of superperiods/FODO periods	**4/12**
Number of dipole magnets/ quadrupole lenses	**32/24**
Magnetic field at injection/maximal field	**0,17/1,8 T**
Rate of magnetic field	**3,26 T/s**
Maximal/injection gradients in F lenses	**8,5/0.8 T/m**
Maximal/injection gradients in D lenses	**–7,5/–0,7 T/m**
Curvature radius in dipole magnets	**3,53 m**
Sagitta in dipole magnets	**8,7 mm**

Betatron tunes	**3,25**
Chromaticity $dQ_x/(dp/p)$	**-3,1**
$dQ_z/(dp/p)$	**-3,2**
Parameter of orbit compaction	**0,053**
COD, mm	**3**
Horizontal/Vertical acceptance, π·mm·mrad	**180/70**
Emittance of injected beam, π·mm·mrad	**10**
Emittances of accelerated beam $\varepsilon_x/\varepsilon_z$, π·mm·mrad	**20/1,5**
Emittance of extracted beam $\varepsilon_x/\varepsilon_z$, π·mm·mrad	**0.5/1,5**
Relative momentum spread	**$\pm 10^{-3}$**
Relative maximal momentum spread	**$\pm 2\times10^{-3}$**

Superconducting Carbon GANTRY



The high technology industrial centers should provide construction of large scale equipment like carbon gantry, provide precision welding and high quality machining of this equipment.

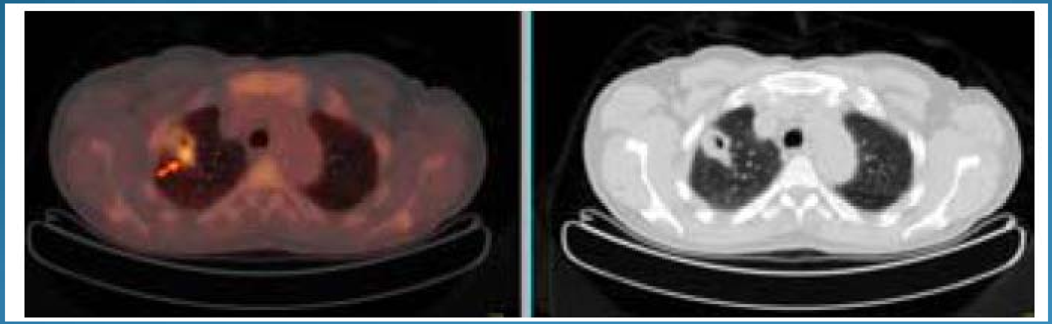
The project is developed in collaboration with “Almas-Antej” where such experience exist. Basics of the project were reported to the Working Group and Technical Council of Russian Ministry for Trade and Industry.

Superconducting Carbon Gantry in Archade project	
Weight, t	156
Diameter, m	9.2
Length, m	12,7
Scanning area in isocenter, cm	20×20
Gantry rotation angle, degree	180
Positioner rotation angle, degree	180
Main dipole magnet	
Magnetic field, T	3.2
Bending radius, m	2
Weight, t	28

Carbon treatment and on-line dose verification with $^{11}C^{4+}$

The use of positron-emitting ^{11}C ion beam could allow to combine both advantages of Carbon treatment and online PET dose verification.

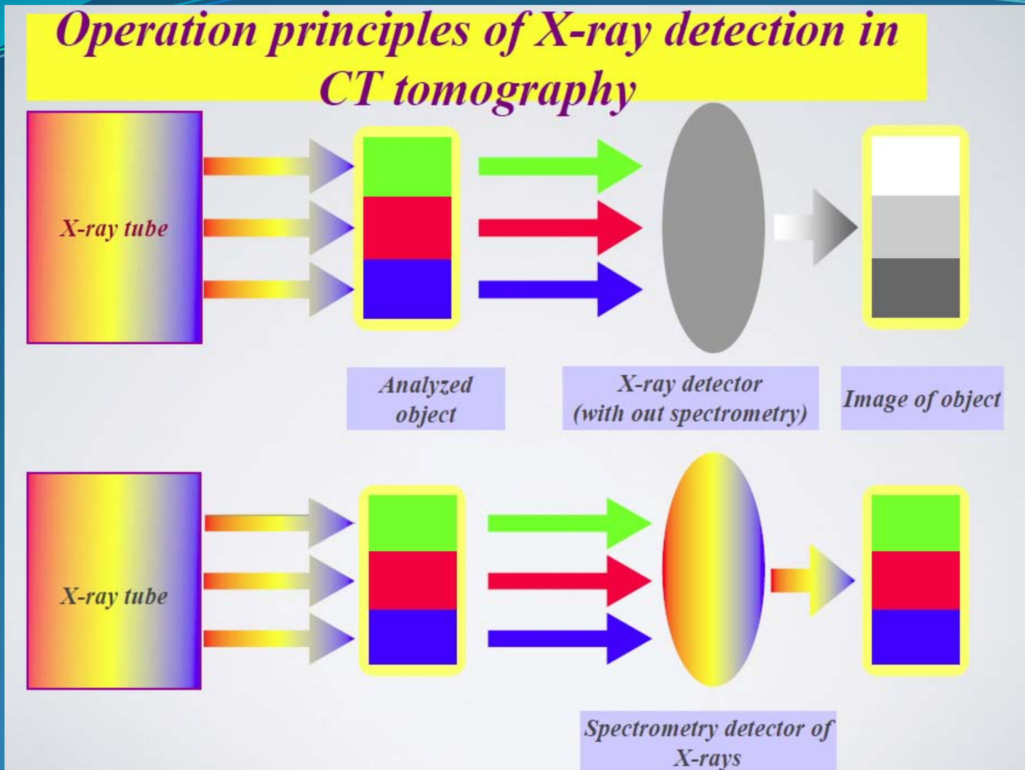
ESIS –Superconducting JINR ion source, applied for carbon ion injection

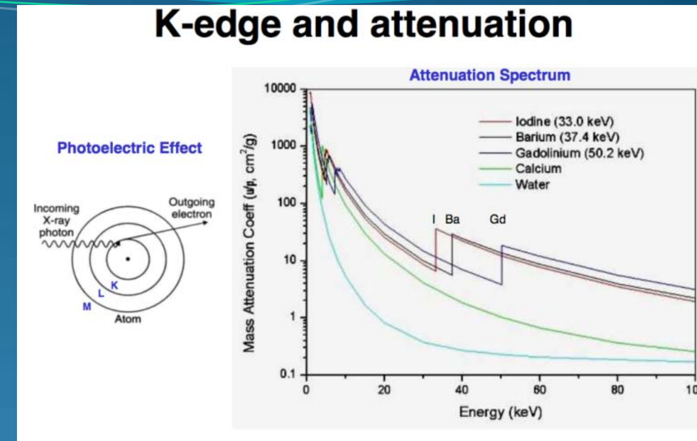


PET/CT and CT images

The technology of formation of primary carbon ion beam in ESIS was proposed and successfully tested by the group of E.Donets from JINR VBLHEP in collaboration with National Institute of Radiological Science (Japan)

Development of pixel semiconductor detectors for CT diagnostics



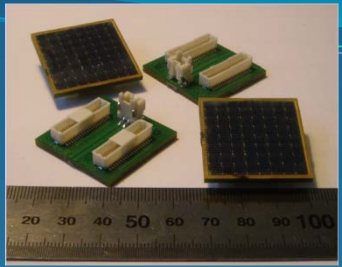


The use of GaAs sensors in CT is very promising for constructing spectrometric CT.

The work at JINR is performed in Collaboration with Tomsk and Dubna Nanotechnological Center.

GaAs pixel detector with pixel size of 50 μm and 65536 channels of electronics

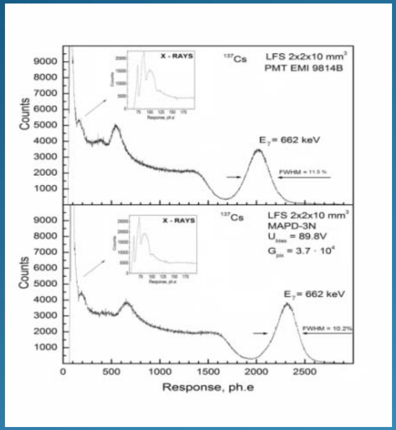
MAPD Application for PET and combined PET/MRI



- High Dynamic Range (pixel densities of up to 40000 mm^2)
- Photon Detection Efficiency up to 30 %
- Gain up to 10^5
- Better radiation hardness
- Insensitivity to magnetic field.
- Compact and rigid
- Low voltage supply (<100 V)

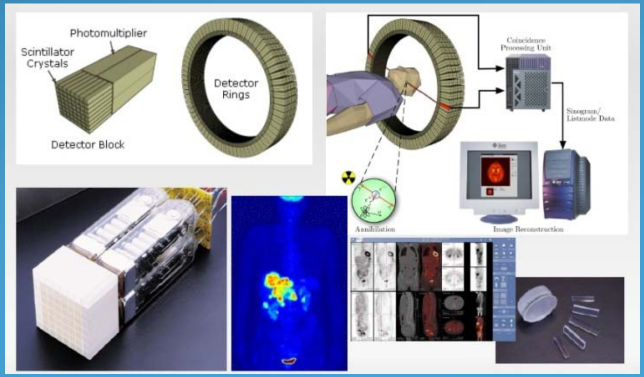
Drawbacks:

- Temperature dependence (a few %%/ºC)
- High dark rate (> 0.5 MHz/mm^2)
- Large Recovery time.



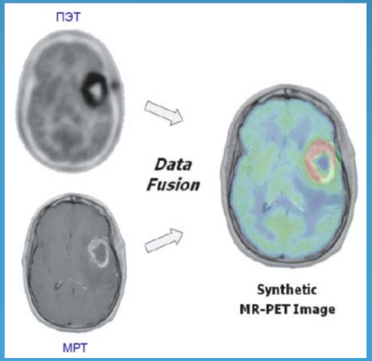
The use of MAPD for PET was already checked and small size and insensitivity to the magnetic field make it promising for the use in combined PET/MRI systems.

The work on MAPD development is performed in the framework of JINR innovation activities in Collaboration with INR (Moscow), Dubna nanotechnological center and others.



Scheme of PET

Single and combined PET and MR images



Conclusions

- ✓ ***The method of 3D conformal proton therapy developed at JINR is effectively used for patients treatment.***

- ✓ ***The transfer of this experience to the wide medical practice is under way. In collaboration with IBA the JINR is participating in the construction of the first Russian Center of Nuclear Medicine in Dimitrovgrad.***

- ✓ ***The construction of other centers in Russia and JINR Member States will profit from this experience. The projects of such centers are under discussion now.***

- ✓ ***There are plans of further development of hadron therapy methods and equipment including superconducting accelerators for carbon treatment and new diagnostic devices. These developments are performed at JINR in a wide international collaboration .***