Acceleration Technique Developed at JINR for Hadron Therapy

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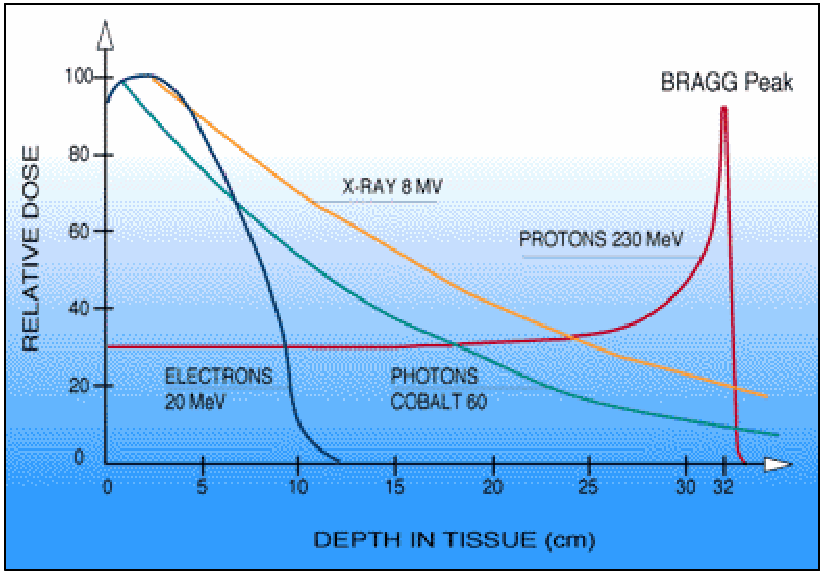
C400 cyclotron team:V.Aleksandrov, S.Gursky, G.Karamysheva, N.Kazarinov, S.Kostromin, N.Morozov, E.Samsonov, G. Shirkov, V. Shevtsov, E.Syresin, A.Tuzikov

Electrostatic storage ring team: E.Syresin, S.Shirkov.

HADRON THERAPY IN WORLD AND IN RUSSIA



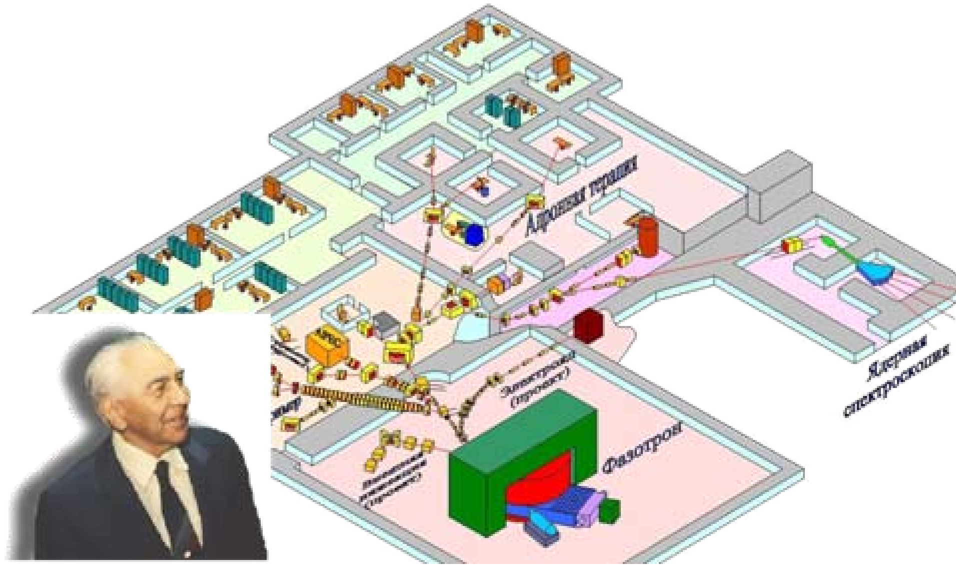
There are about 30 centers of the proton therapy and 5 centers of carbon therapy at the world now. About 100 thousand patients were treated with application of hadron therapy during last 50 years, 60 % of them were treated over last 10 years and 90% of total patients now treated in the hospital based facilities.

2.3 million of tumor patients there are in Russia 450 thousands of new patients are appeared per year.

The proton therapy is recommended 50 thousands of patients per year in Russia.

JINR Medical-Technical Complex on proton beams of synchrocyclotron

1967 – First investigations at cancer treatment;
1968 –1974 –84 patients was 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 radiated by proton beams;
1999, – Creation of radiological department in Dubna hospital;
2000 – 2012, – 883 patients were radiated by proton beam.



During last years around 100 patients per year were radiated by proton beam in JINR Medical-Technical Complex in frame of research program of Medical Radiological Research Center of Russian Medical Academy of Science.

More than 1000 patients were treated by the JINR proton beams

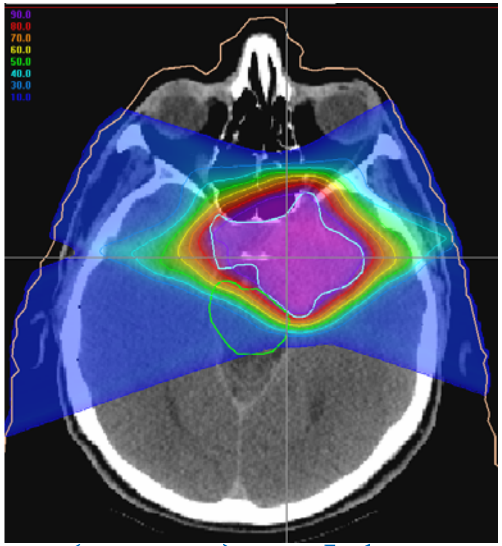
JINR PHASOTRON MEDICAL PROTON BEAMS

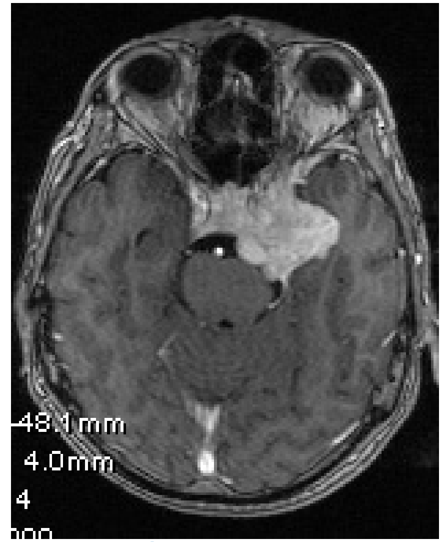
Cancer treatment in cabin №1

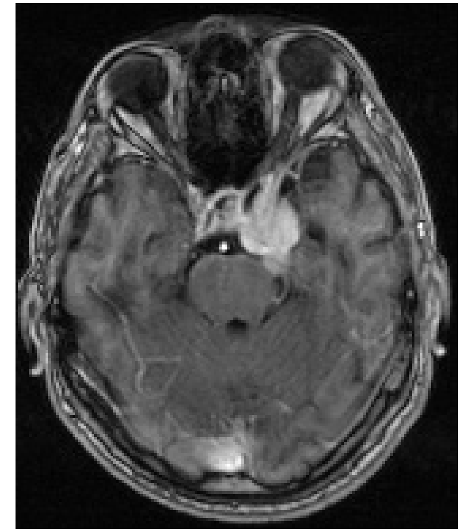
3D conformal proton beam treatment were realized in Russia only in JINR.

3D conformal proton therapy in JINR

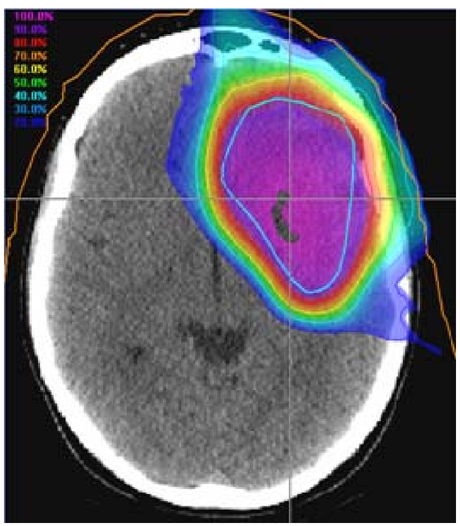
Plan of proton treatment of meningiomas

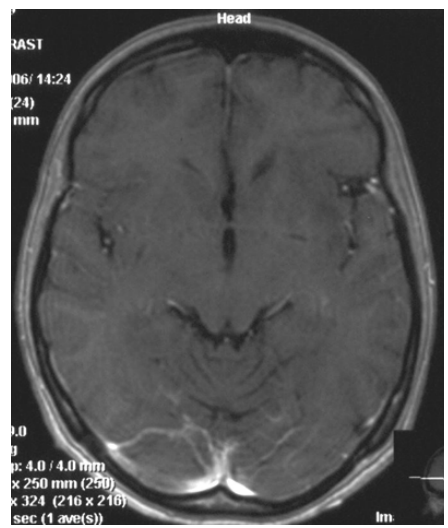






MRI before treatment(center) and 1 year later after treatment (right)large reduction of meningiomas volume





Treatment of brain astrocytomas by proton beams

JINR treatment by medical proton beams in 2000-2012

Meningiomas (Менингиомы)	157
Chordomas, chordosarkomas (Хордомы и хондросаркомы основания черепа)	28
Chordomas (Хордома позвоночника)	3
Gliomas (Глиомы)	54
Lymphoma (Лимфома)	1
Acoustic Neurinomas (Невриномы слухового нерва)	14
Astrocytomas (Астроцитомы)	38
Paragangliomas (Параганглиома)	6
Pituitary Adenomas (Аденомы гипофиза)	23
AVMs (Артерио-венозные мальформации)	71
Brain and other metastasis (Метастазы в мозг)	72
Other head and neck tumors (Опухоли головы и шеи)	238
Melanomas (Меланомы)	14
Skin diseases (Рак кожи)	51
Carcinoma metastasis of the lung (Опухоли легких)	7
Breast cancer (Рак молочной железы)	48
Brain cancer (Опухоли мозга)	8
Prostate Adenomas (Рак простаты)	1
Sarcomas (Саркомы)	15
Other (другие)	34
Total	**883**

Federal High Technology Center of Medical Radiology
(Dimitrovgrad, Ulyanovsk reg.)

E.Syresin et al, IPAC11, p.2706.

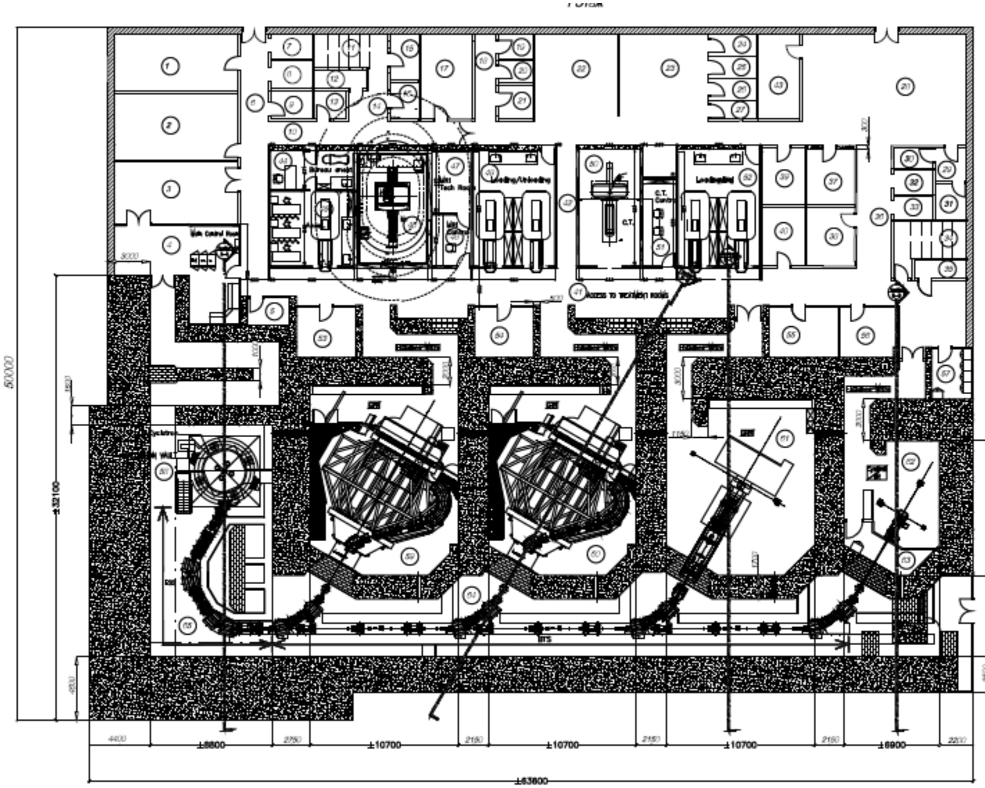
The Federal high technology center of medical radiology involves:
Center of Proton therapy
PET Center

The center consists of two gantry systems, a medical treatment room with a fixed beam, an eye treatment room and a PATLOG system of preliminary patient positioning.

The JINR-IBA collaboration has developed and constructed the C 235-V3 proton cyclotron for this center.

Equipment of Dimitrovgrad proton center for proton therapy was certificated first time in RF.

The Project of the Center of proton therapy was developed by Federal Medico-Biological Agency in collaboration with JINR



Planed Centers of Proton Therapy, realized in frame of Russian Federal program:

- Dimitrovgrad
- Obninsk
- Tomsk

Production of medical proton cyclotron in JINR

E.Syresin et al, Physics of Particle and Nuclear Letters,2011, v. 8 p.379

JINR-Ion Beam Application (IBA, Belgium) collaboration since 2007 starts development of essentially modified version of IBA serial cyclotron C235 so called cyclotron C235-V3 applied for hospital centers of proton therapy.

C235-V3 cyclotron is superior in its parameters to the IBA C235 serial medical proton cyclotron of previous generations installed in 16 hospital centers in the world.

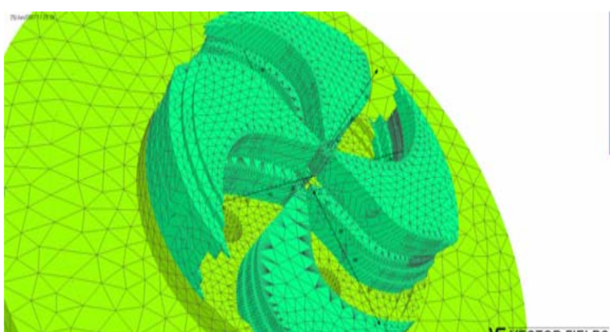
The further improvement of cyclotron C235-V3 parameters is expected also in frame of JINR-IBA research works proposed by JINR

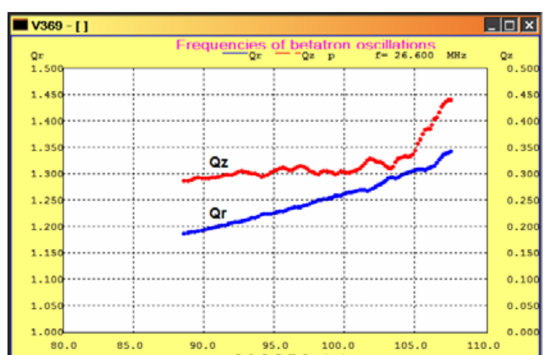
2010–C235-V3 construction was completed

June 2011 г. – Start of assembling and tests of cyclotron in Dubna

September 2012 - Delivery of cyclotron in Dimitrovgrad hospital center of proton therapy

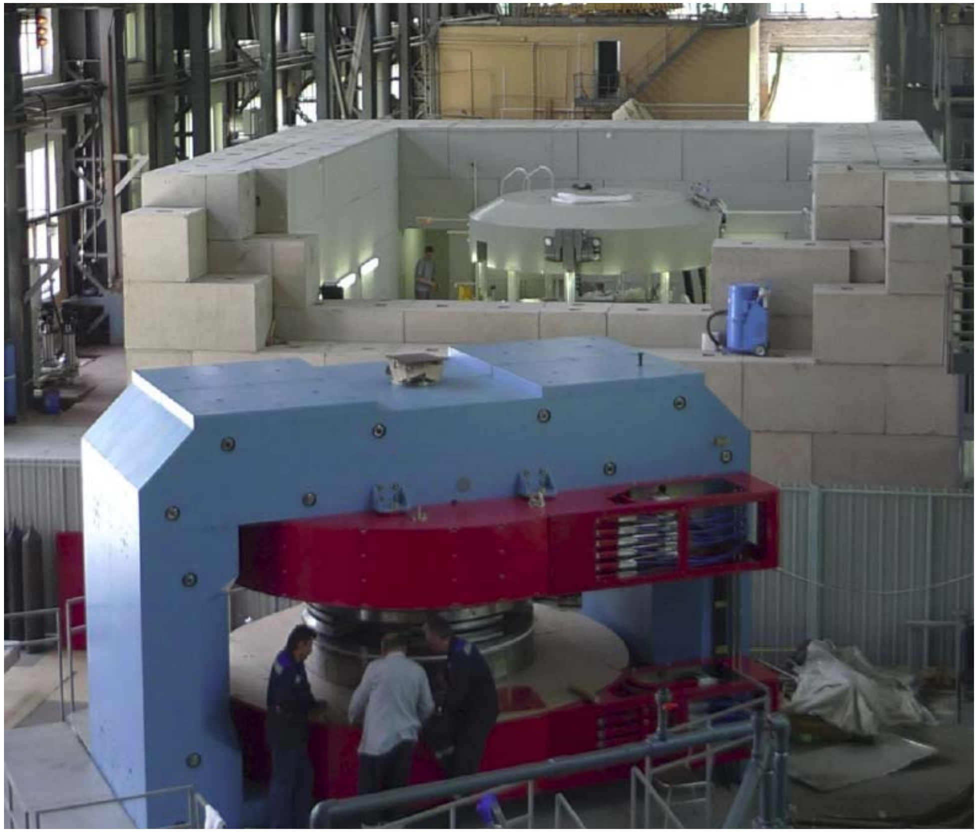
Accelerators for JINR members countries





Cyclotron C235-V3 produced by JINR-IBA collaboration

General parameters	Value
Proton energy, MeV	235
Internal current, nA	300
Beam emittances, π·mm·mrad	12/11
Magnetic field (min/max) T	0.9/2.9
Number of sectors	4
Magnet diameter, m	4.3
Radius of beam extraction, m	1,08
Elliptical hill gap, cm	9,6/0,9
Duant aperture, cm	2
RF frequency, MHz	106.1 (4 harmonic)
Dee voltage, (min/max) kV	60/130
Ion source	PIG, internal
Electrostatic deflector field, kV/cm	170
Extraction efficiency, %	60
Power, kW	446
Weight, t	220

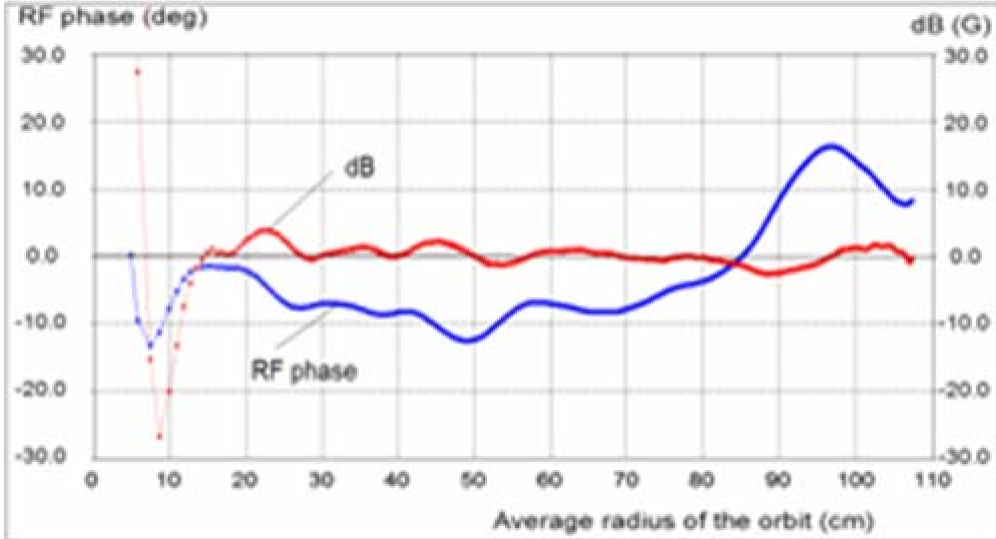


JINR engineering center for assembling and tests of medical accelerators.
FLNR JINR Cyclotron for filter production applied for blood plasmoferese (forward plan).
DLNP JINR cyclotron for proton therapy (behind plan)

Medical proton cyclotron C235-V3 in JINR

Shimming of JINR-IBA medical cyclotron C235-V3

S. Kostromin RUPAC12,FRBCH001



Difference between formed and isochronous field (red), integrated RF-phase shift (blue).

New technologies realized in JINR at magnetic shimming of C235-V3

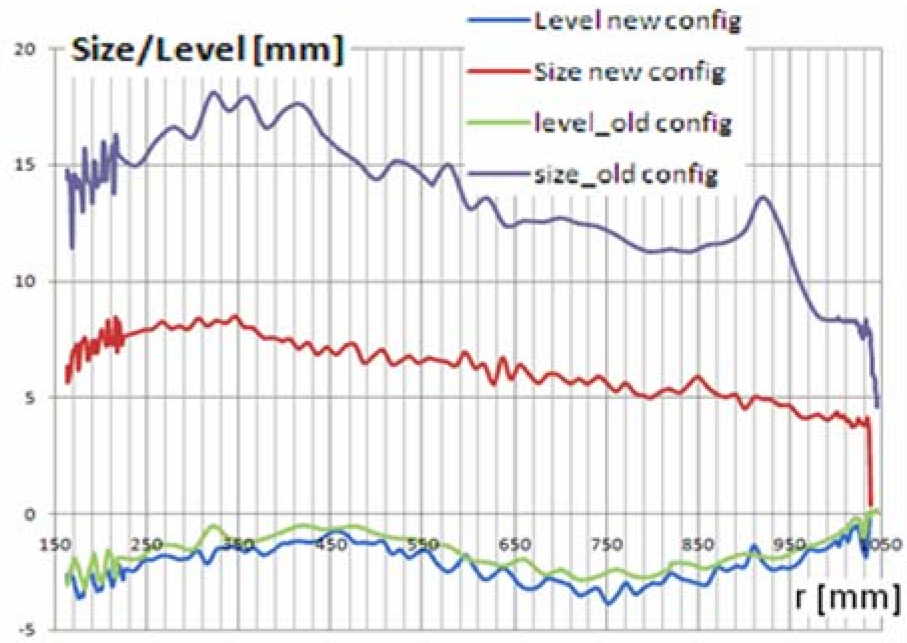
Special platform for mechanical fabrication with diameter of 1 m was constructed instead IBA platform diameter of 2 m

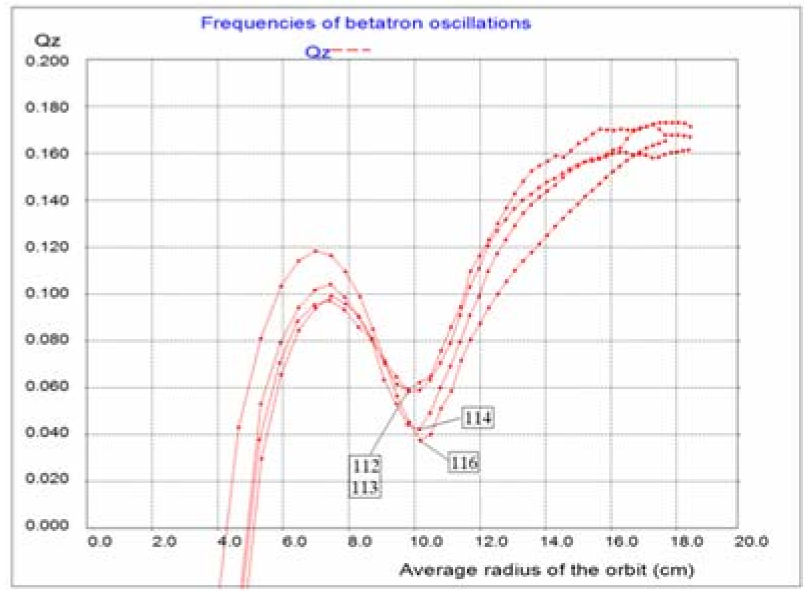
Special 3D Carl Zeiss machine provided sector edge surface measurements with μm accuracy was incorporate in shimming technology

The new JINR 2.9 T calibration dipole magnet instead 2.5 T IBA magnet

The new system for measurement of the average radial component

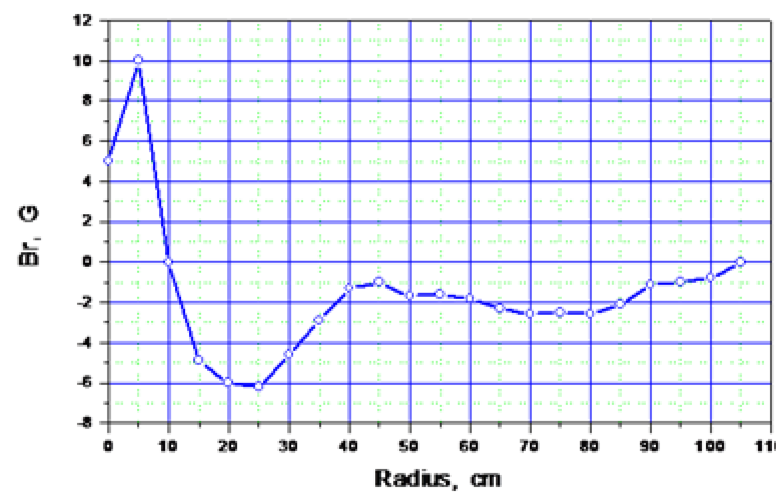
Beam Tests of JINR-IBA cyclotron C235-V3





Qz-drop at 100mm in C235-V3

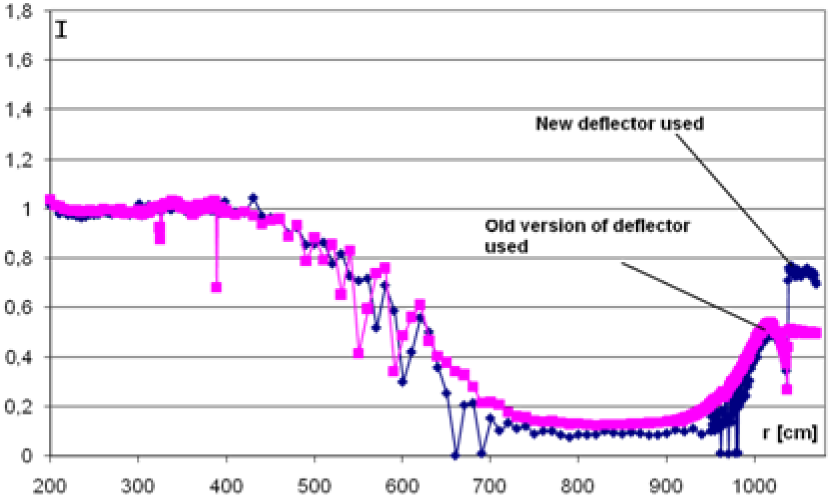
Amplitude of axial incoherent oscillations and axial coherent beam displacement before and after correction correction of Qz-drop at 100mm



Average radial Br component

Transmission from r=300mm to 1030 mm is 72%. Then circulating beam was extracted by the electrostatic deflector (60kV voltage, 3mm deflector gap). Extraction efficiency is 62%. Thus, the total efficiency of C235-V3 is 45%.

MODIFIED CYCLOTRON C235-V3



Improvement of extraction efficiency from 50% to 75% with new extraction system

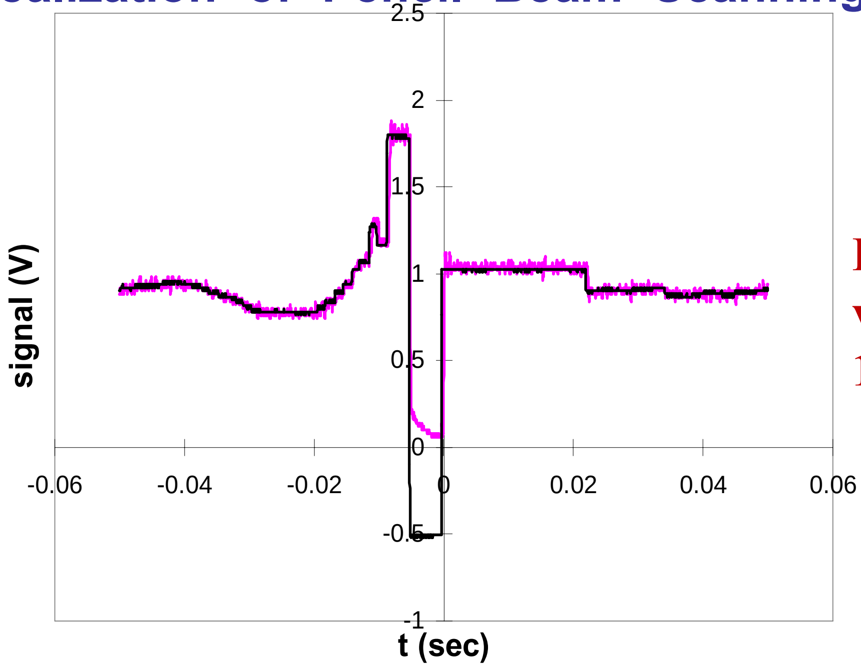
Parameter	C235	C235-V3
Optimization of magnetic field at modification of sector	no	Modification of sector azimuthal angle at R>80
Vertical betatron frequency at R>80	Qz=0,25	Qz=0,45
Vertical coherent beam displacement related to median plate effects	4 mm	2-3 mm
Beam losses at proton acceleration with out installed diaphragm	50%	25%
Beam losses at extraction	50%	25%
Br-component measurements, reduction of median plane effects	No	yes
Reduction of radiation dose of cyclotron subsystems		by 2-3 times

Advantages of C235-V3 with high intensity of proton beam are important:

* at treatment of large volume tumors with application of pencil beam scanning system;
* at treatment technology with large dose per irradiation fraction and small number of fractions;
* at reduction of radiation dose of cyclotron subsystems at operation

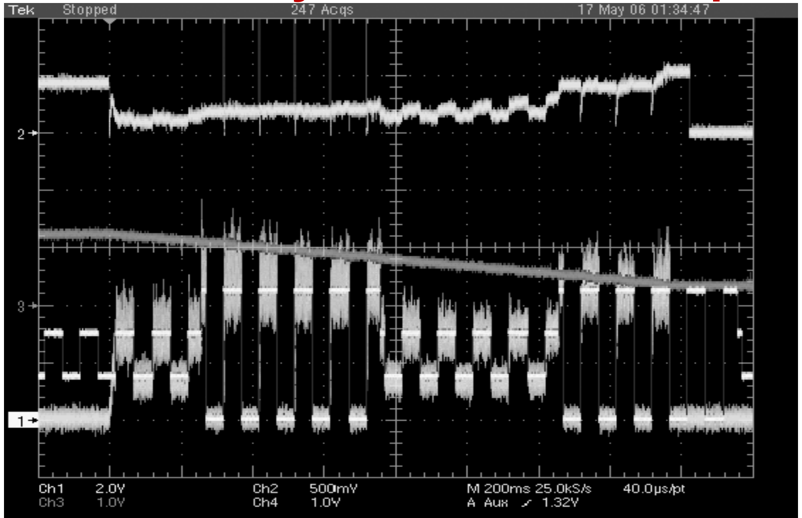
BEAM CURRENT MODULATION

The current modulation of extracted proton beam at a frequency up to 1 kHz gives main advantage at realization of Pencil Beam Scanning (Intensity Modulated Proton Therapy)



Beam modulation by vertical deflector plate at 1 turn.

Beam intensity variation in IBA proton cyclotron C235

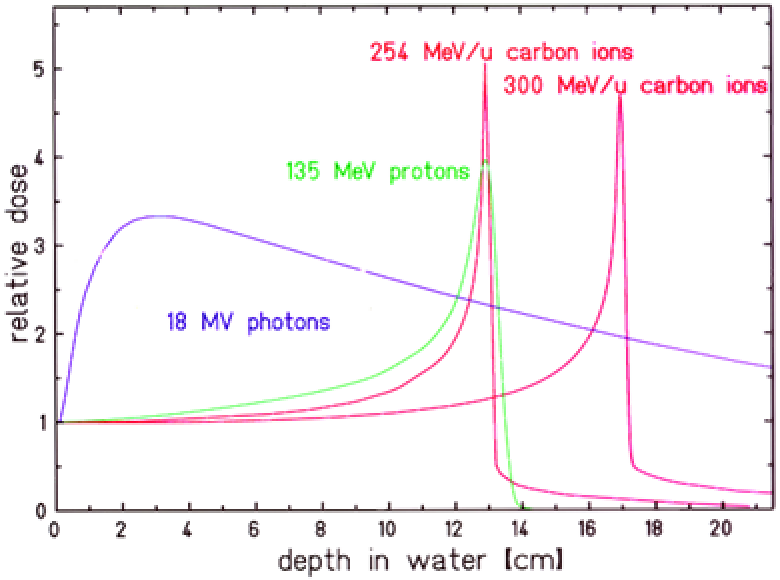


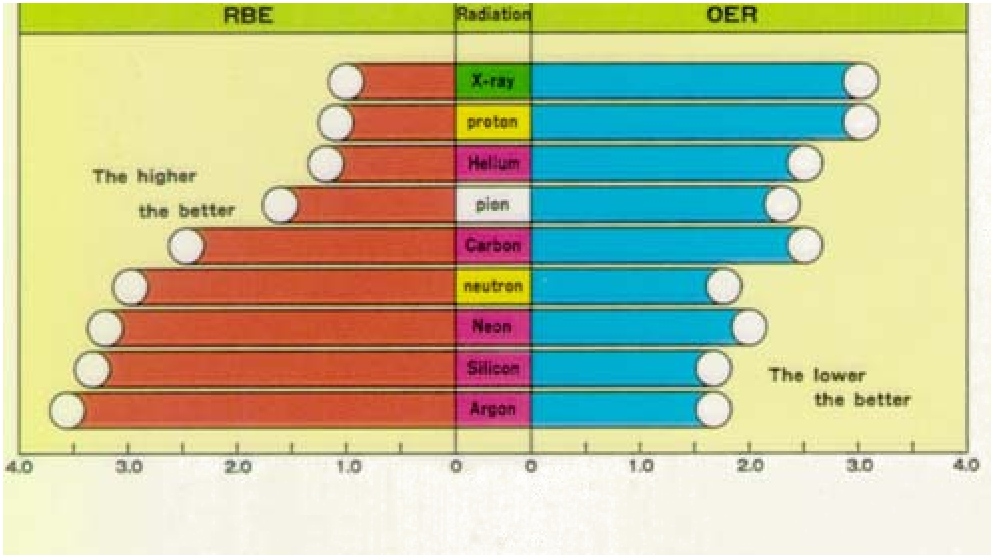
Three steps of beam intensity variation at HIMAC RF-knockout extraction technique in medical synchrotrons provides beam intensity modulation up 1 kHz.
However the spill ripple is around ±10% in this case

Proton –ion therapeutic complex (PITC) applied for carbon ion therapy

Adventures of ion carbon therapy:

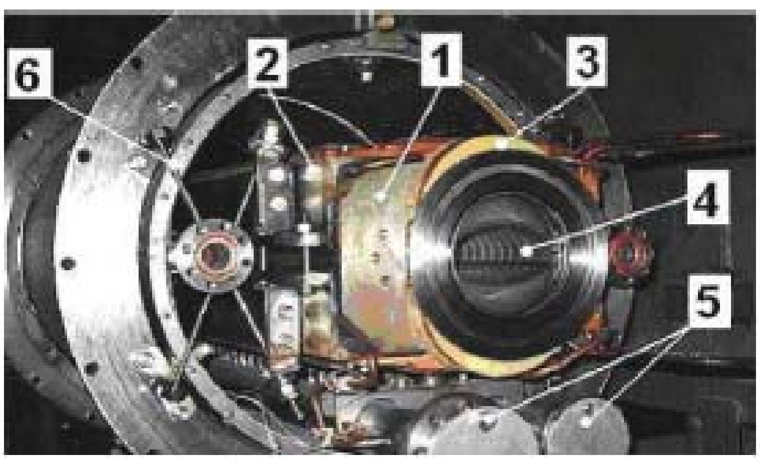
- Carbon ions are especially efficient for radio resistant tumors
- Carbon ions produces by 4 times less dose irradiation of normal tissues comparing with X-ray radiation, at same irradiation dose in tumor.
- Carbon ions produces by 2 times less dose irradiation of normal tissues comparing with protons.





Nuclotron technologies as basis of superconducting medical synchrotron for hadron therapy

Nuclotron –JINR superconducting synchrotron

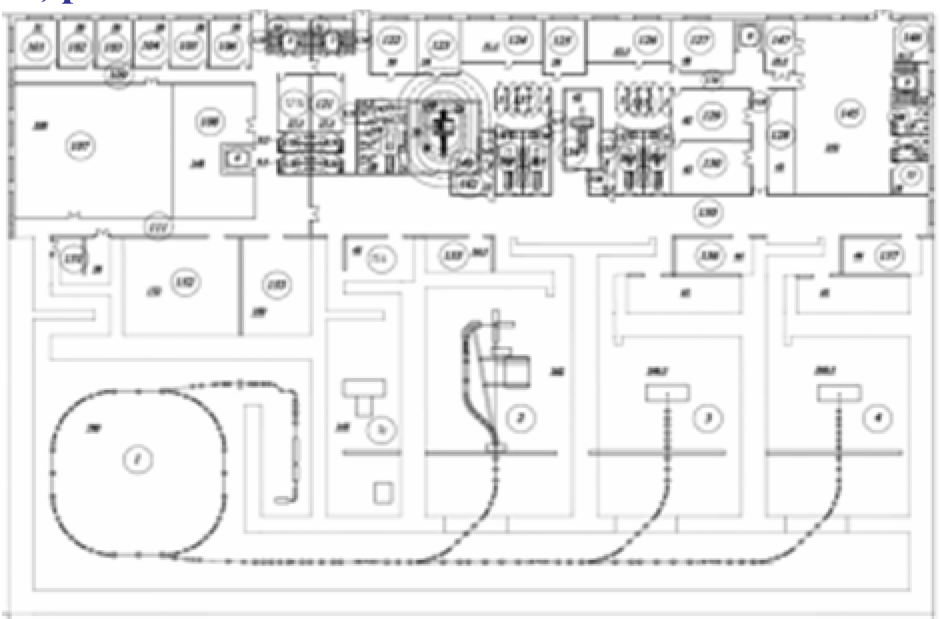


Nuclotron superconducting dipole magnet

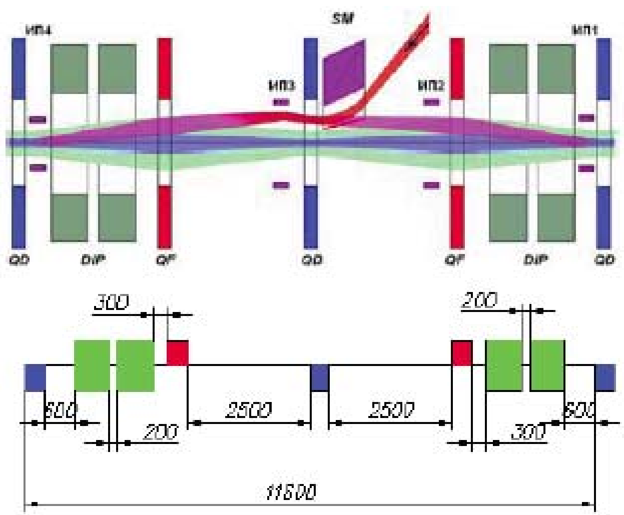
Parameters of medical synchrotron	
Ion source	*«Krion»*
Linear accelerator	*RFQ &IH*
Circumference	*69.6 m*
Injection energy	*4 MeV/n*
Max. ion energy at A/Z=0.5	*400 MeV/n*
Max. magnetic field n	*1,8 T*
Magnetic field rate dB/dt	*3.6 T/s*
Repetition frequency	*1 Hz*

Complex of ion therapy on the basis of superconducting synchrotron

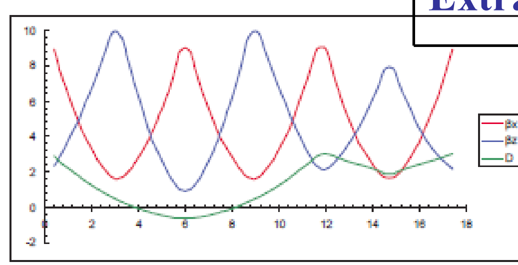
E. Syresin et al, Physics of Particle and Nuclear Letters, 2012, v.9, p.328

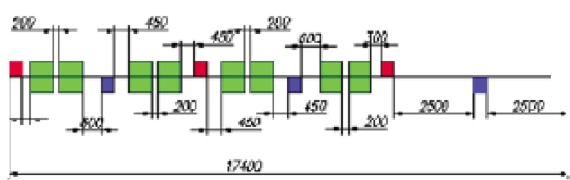


Injection/maximal energy	4,2/400 MeV/u
Maximal/ injection magnetic rigidity	6,36/0.59 T·m
Circumference	69,6 м
Column limit of intensity at injection	$6 \cdot 10^9$ p/cycle
Betatron tune shift	0,02
Number of turns at injection	20
Injection efficiency	50 %
Time of synchrotron acceleration	0.5 s
Slow extraction time	(0,5 -10) s
Extraction efficiency	96%

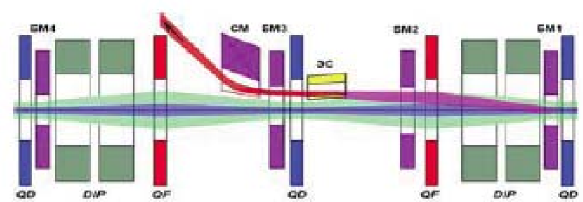


Multiturn injection in synchrotron





Superperiod of synchrotron



Extraction from synchrotron

Parameters of medical ion synchrotron

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	$\pm 2\times10^{-3}$

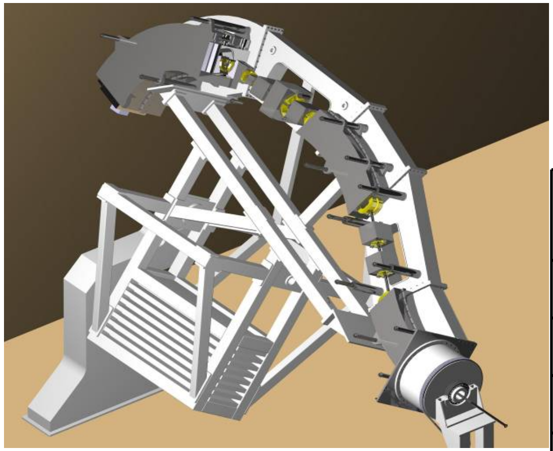
Number of superperiods/FODO periods	4/12
Number of dipole magnets/ quadrupole lenses	32/24
Magnetic field at injection/maximal field	0,17/1,8 T
Rate of magnetic field	3,26 T/s
Maximal/injection gradients in F lenses	8,5/0.8 T/m
Maximal/injection gradients in D lenses	–7,5/–0,7 T/m
Curvature radius in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

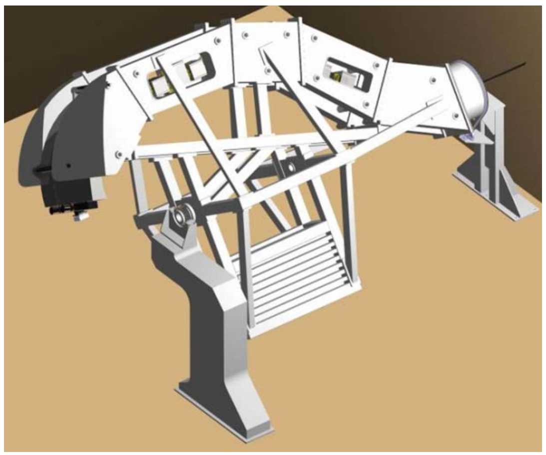
Beam delivery system

The beam delivery system consists of following sections:
the extraction section;
the foil section provided equal beam emittances in both transverse planes;
the accommodation section;
the section for beam delivery in the cabin;
the section of beam transportation between the medical cabins;
the isocentric gantry;
the channel with fixed beam position cabin.

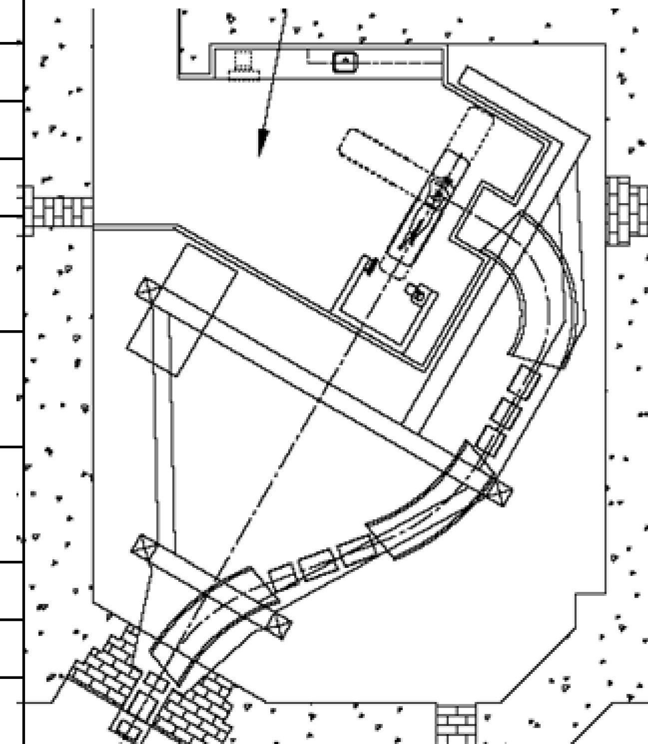
The compact carbon gantry

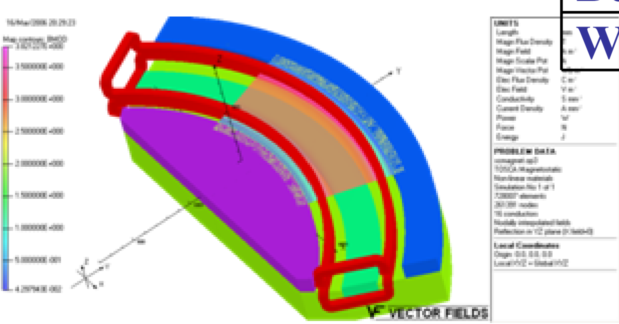
JINR-IBA collaboration



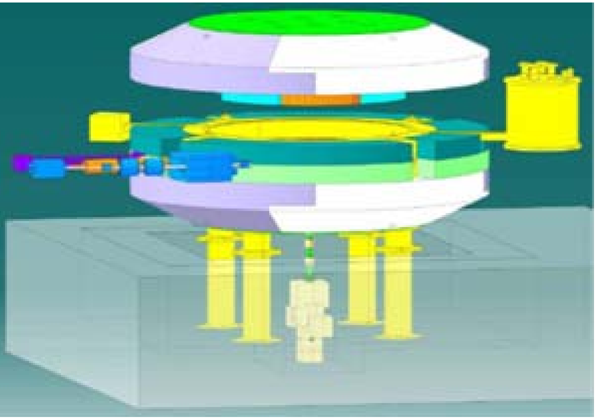


Gantry	
Weight, t	156
Diameter, m	9.2
Length, m	12,7
Scanning area in isocenter, cm	20×20
Gantry rotation angle, degree	180
Positioner rotation angle, degree	180
Main dipole magnet	
Magnetic field, T	3.2
Magnetic field rate, T/min	1
Bending radius, m	2
Weight, t	28

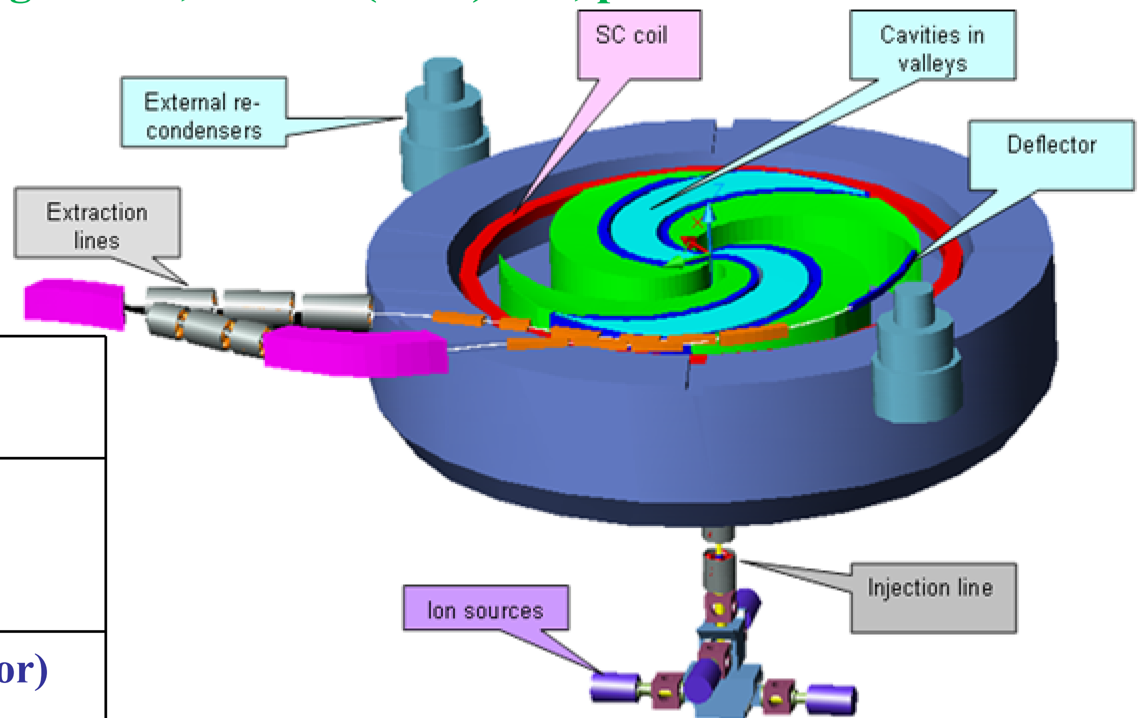




The application of superconducting gantry permits to increase number of recommended for carbon treatment cases from 7% up 30%



Y. Jongen et al, NIM A (2010) 624, p.47



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

Superconducting cyclotron C400 developed by JINR-IBA collaboration

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

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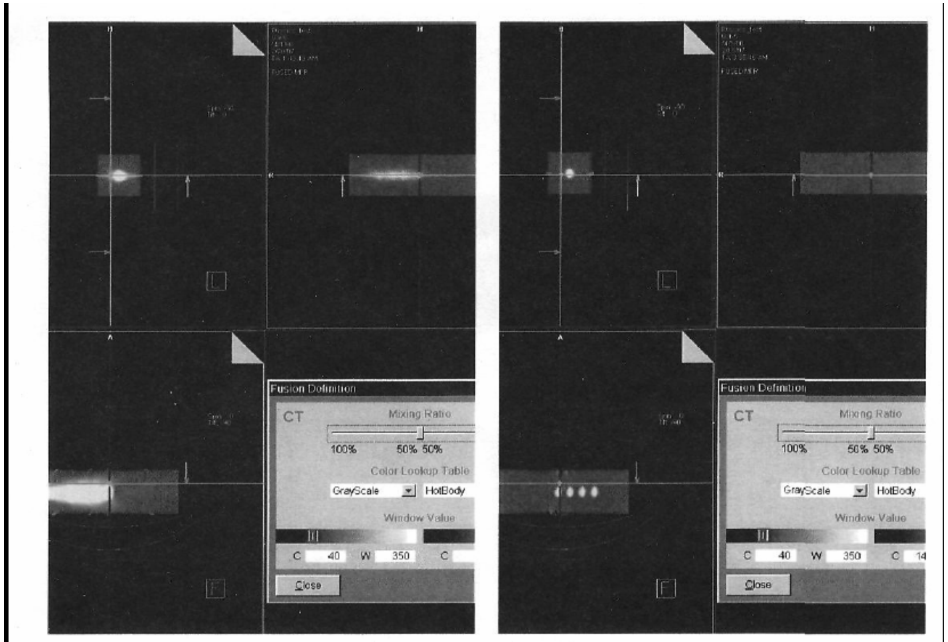
Carbon treatment and on-line dose verification at application of primary radioactive ions $^{11}C^{6+}$

JINR-National Institute of Radiological Science (NIRS, Japan) collaboration

E.D. Donets et al, IPAC10, THPEC066.

- On-line dose verification at carbon treatment by high intensive radioactive $^{11}C^{6+}$ ion beams
- High radioactive ion intensity $^{11}C^{6+}$ required for cancer treatment and simultaneously on-line PET tomography
- High resolution at direct application of primary radioactive $^{11}C^{6+}$ ion beam comparing with radioactive secondary beams produced in tumor target.

secondary $^{11}C^{6+}$ beams primary $^{11}C^{6+}$ beams



Electron String Ion Source (ESIS) for production of radioactive ions $^{11}C^{6+}$ applied simultaneously for carbon treatment and PET

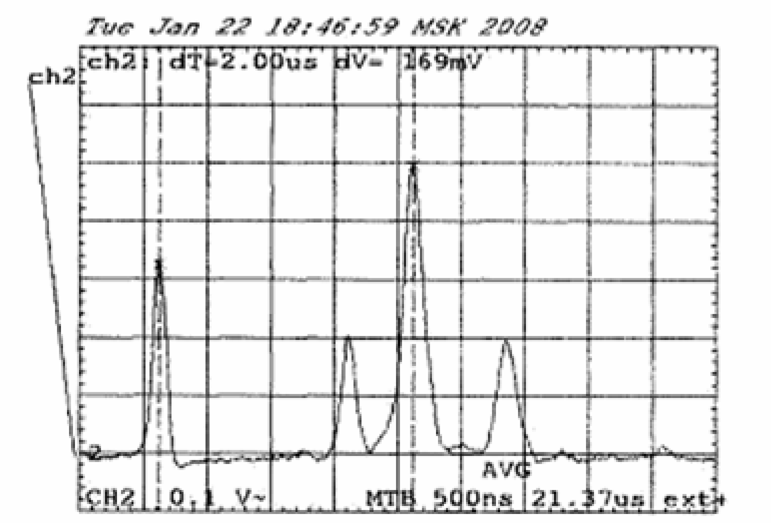
LPhHE, JINR at leadership of Prof. E.Donets

E.Donets, RUPAC12, FRYOR02

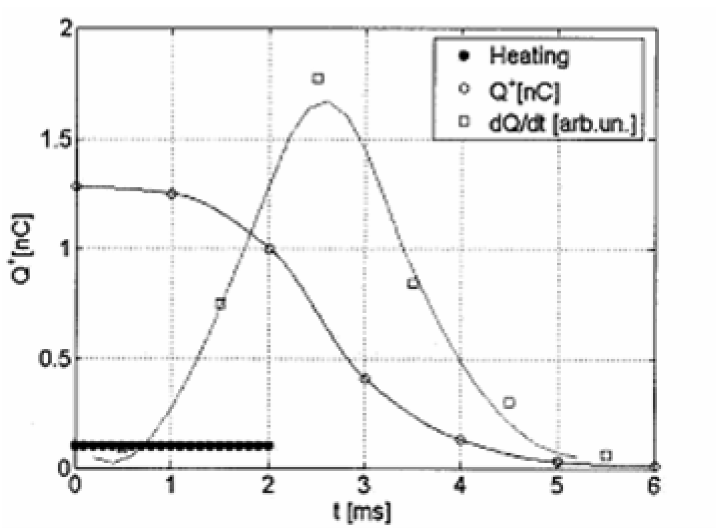
- Realization of ISOLDE scheme for formation of radioactive ion ^{11}C beams
- Production and separation of radioactive gas containing isotope of ^{11}C
- Radioactive gas loading in ESIS at an intensity of 5×10^{12} molecules with a repetition time of 20 min
- Extraction of radioactive ion beam at an intensity of 5×10^{9} ppp of $^{11}C^{4+}$ or $^{11}C^{6+}$
- Conversion efficiency of molecules contained ^{11}C into $^{11}C^{4+}$ corresponds to 25-30% and 15% into $^{11}C^{6+}$

Ion source	Krion-2 C^{4+}	Krion-5T C^{4+}
Electron energy, keV	3-5	5-7
Number of electrons	$6\cdot10^{10}$	$3\cdot10^{11}$
Magnetic field, T	3	5
Number of extracted ions per pulse	$2\cdot10^{9}$	$6\cdot10^{9}$
Injection frequency, Hz	0.3-1	0.3-1
Gas pulse injection time, ms	2	1
Ionization time, ms	6	2

Project parameters of primary radioactive carbon ion beam produced at ESIS injection in HIMAC



Spectrum of charged ions (H+, C5+, C4+, C3+ pics).



Ion charge and its derivative versus of time at 2 ms heating pulse and ion accumulation-ionization time 10 ms.

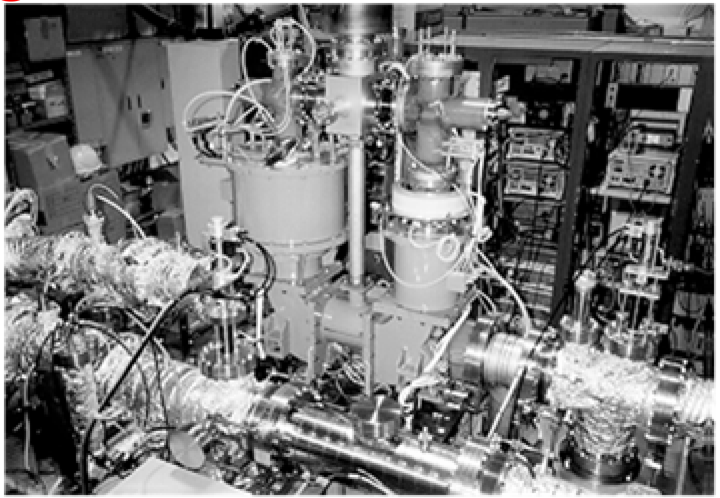
Project parameters of primary radioactive carbon ion beam produced at ESIS injection in HIMAC

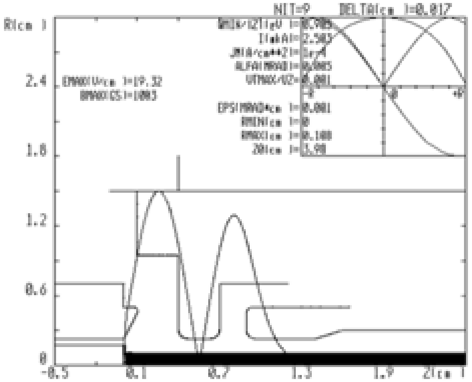
Methane target	
Number of produced $^{11}CH_4$ molecules	$4 \cdot 10^{12}$
Methane loading cycle, min	20
Ion source parameters	
Number of methane molecules used per pulse injection	$4 \cdot 10^{10}$
Methane conversion efficiency into ions, %	15
Number of produced ions per pulse	$6 \cdot 10^{9}$
Linac	
Linac and striping efficiency of $^{11}C^{4+}$,%	80
Injection current, μA	45
Injection emittance at 6 MeV/u, π·mm·mrad	2
Number of injection turns	30
Injection time, μs	120
Injection efficiency, %	60
Synchrotron	
Number of ions in coasting mode	$2.8 \cdot 10^{9}$
Horizontal emittance, π·mm·mrad	80
Number of accelerated ions	$2.2 \cdot 10^{9}$
Number of ions produced for scanning irradiation per injection-extraction cycle	$2 \cdot 10^{9}$
Number of extracted ions per second	10^{8}

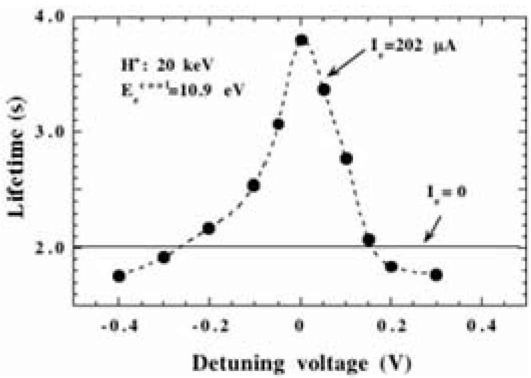
Formation of low energy electron and biomolecular ions in electrostatic ring

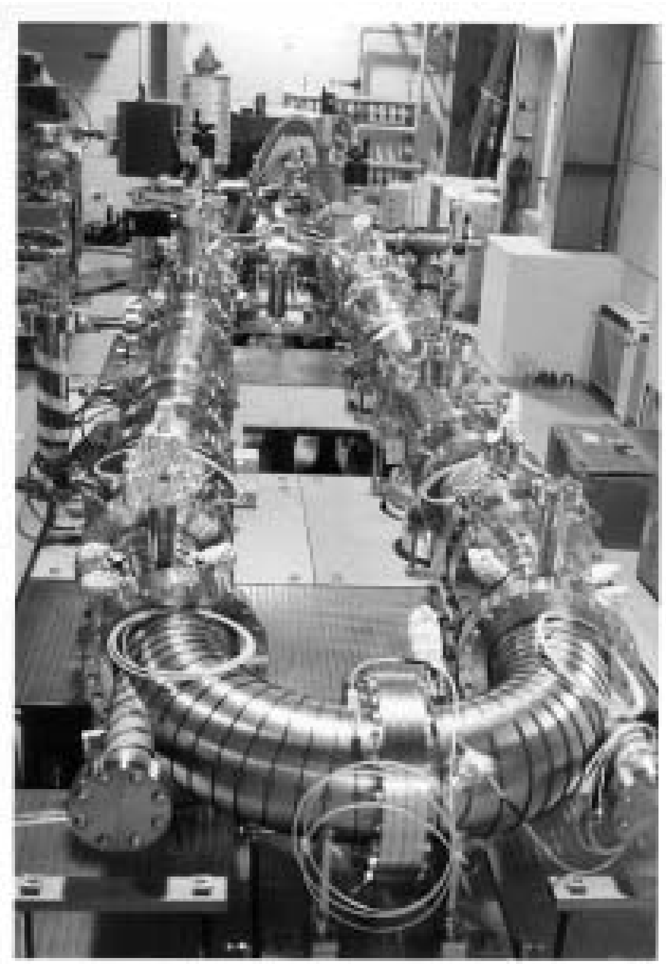
JINR-NIRS (Japan) collaboration

T.Tanabe, K.Noda, E.Syresin, NIMA 532 (2004) p.105
E.Syresin, S.Shirkov, Phys. of Particle and Nuclei Letters (2011), v.8, p.978

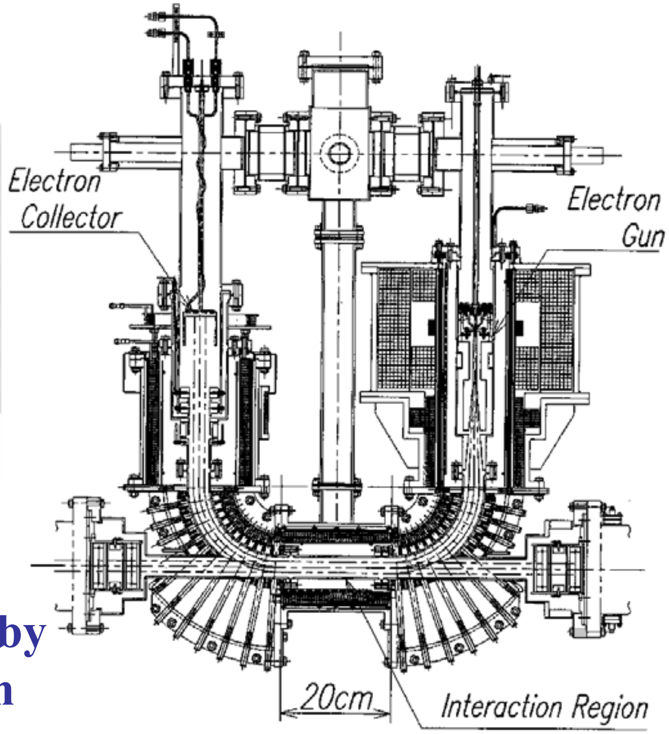








KEK electrostatic ring

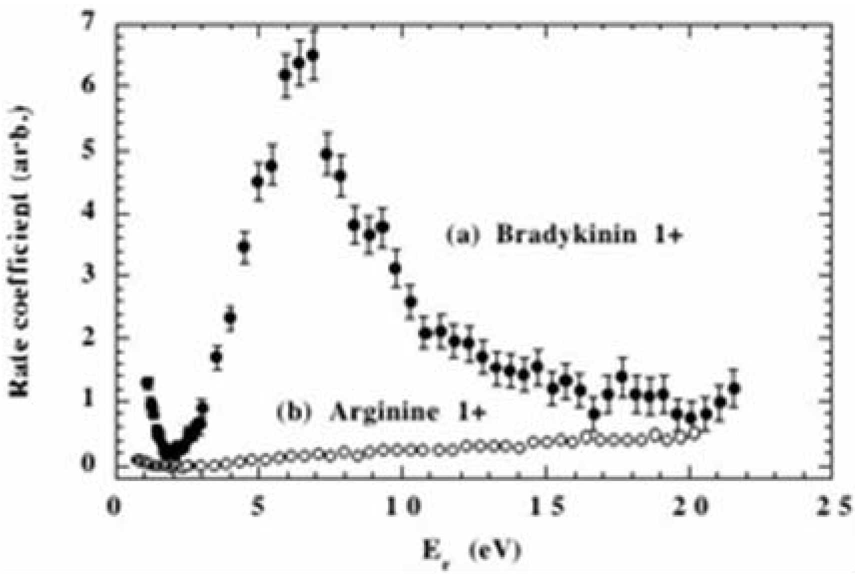


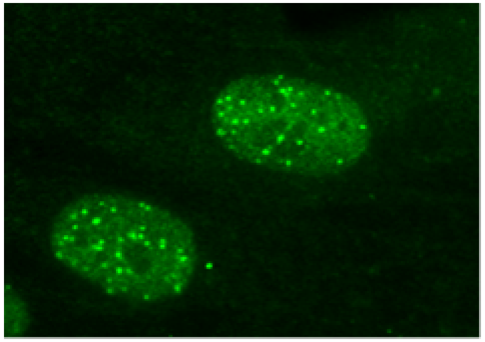
Electron target developed by JINR-NIRS collaboration

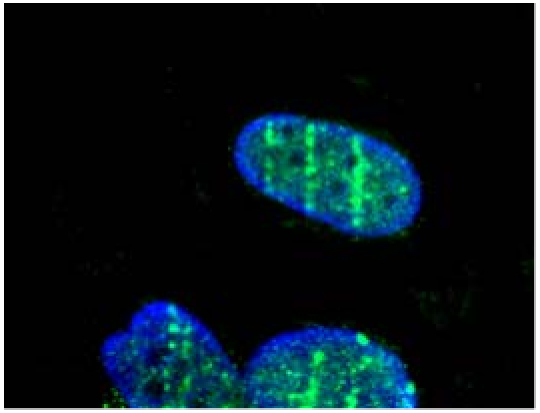
Interaction of low energy electron and biomolecular ions in electrostatic ring

JINR-NIRS (Japan) collaboration

Interaction of the delta-electrons with DNA molecules is one of the important mechanisms realized in process of the hadron therapy.





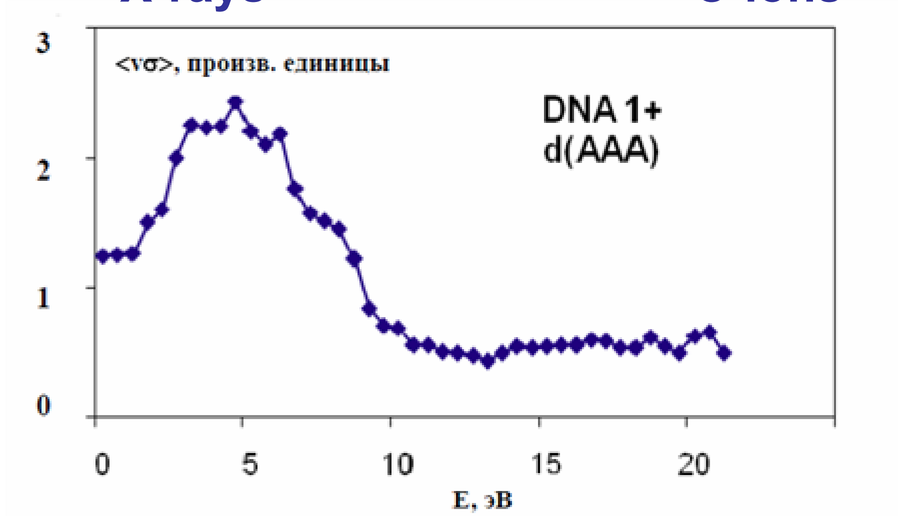


Double strand break of DNA at irradiation of

X-rays C-ions

Neutral production particle rate as a function of relative energy .

Arginine (Arg) (MW: 0.17 kDa) - amino-acid;
bradykinin (MW: 1.06 kDa)- peptide which consists of 9 amino-acids



Interaction of electrons with DNA ions

THANKS FOR YOU ATTENTION