CENTERS OF HADRON THERAPY ON THE BASIS OF CYCLOTRONS

E.M.Syresin,

Joint Institute for Nuclear Research, Dubna, Russia

JINR MEDICAL TECHNICAL COMPLEX

REQUREMENTS TO MEDICAL PROTON BEAMS

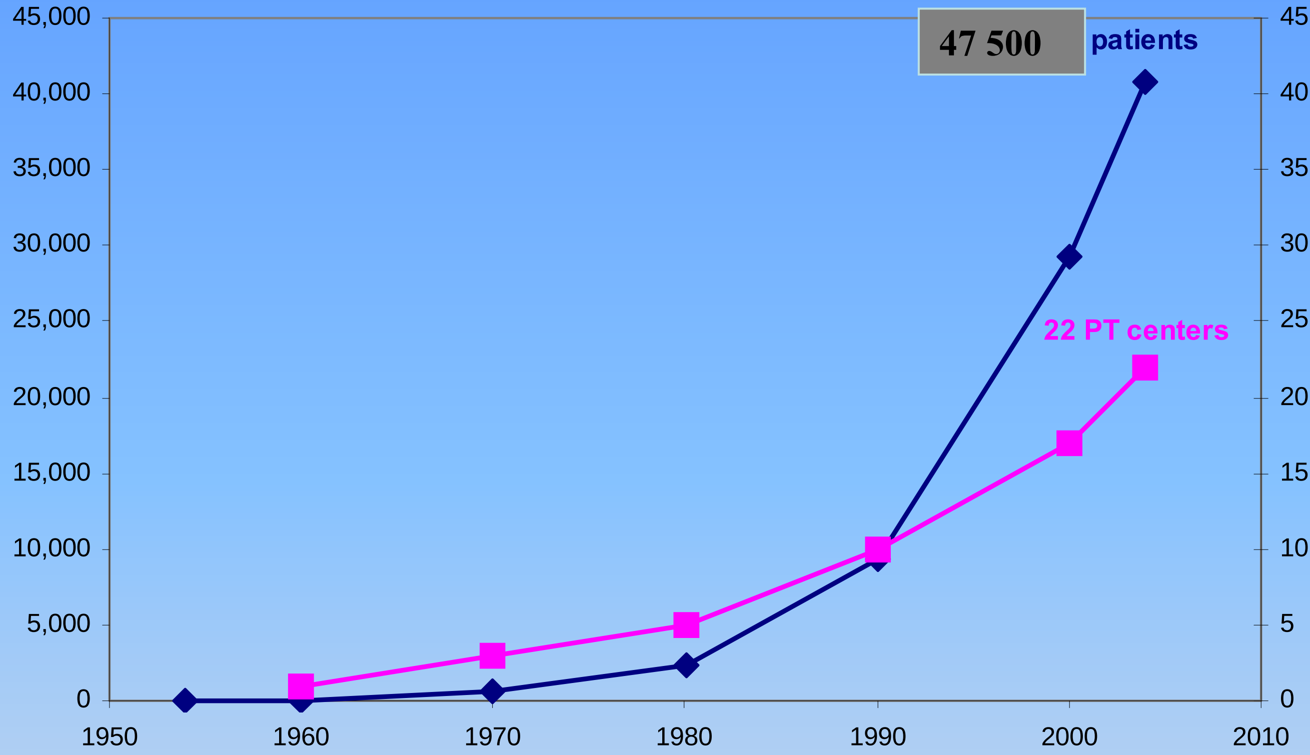
CYCLOTRON CENTERS OF PROTON THERAPY

DUBNA CYCLOTRON CENTER OF PROTON THERAPY

CYCLOTRON CENTERS OF CARBON THERAPY

FORMATION OF CARBON RADIOACTIVE PRIMARY BEAMS

HADRON THERAPY IN WORLD AND IN RUSSIA



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

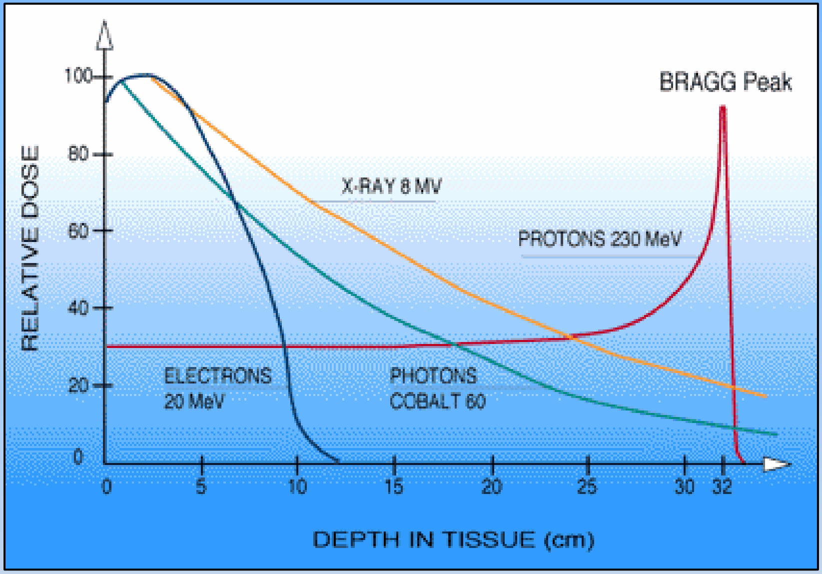
The proton therapy is recommended 50 thousands of patients per year in Russia.

The present Russian research centers of proton therapy provide cancer treatment only for 1 % of patients.

DEPTH DOSE DISTRIBUTION

$$\Delta E = 2\xi \ln\left(\frac{E_{max}}{I} - \beta^2\right) \qquad \xi = 0.15\frac{MeV\,cm^2}{g}\frac{Z_i^2}{\beta^2}\frac{Z_t}{A_t}\rho x$$

***ρ - density, x – target thicknes, Z_i- ion charge, Z_t u A_t -charge and atomic number of target*, I – ionization potential**

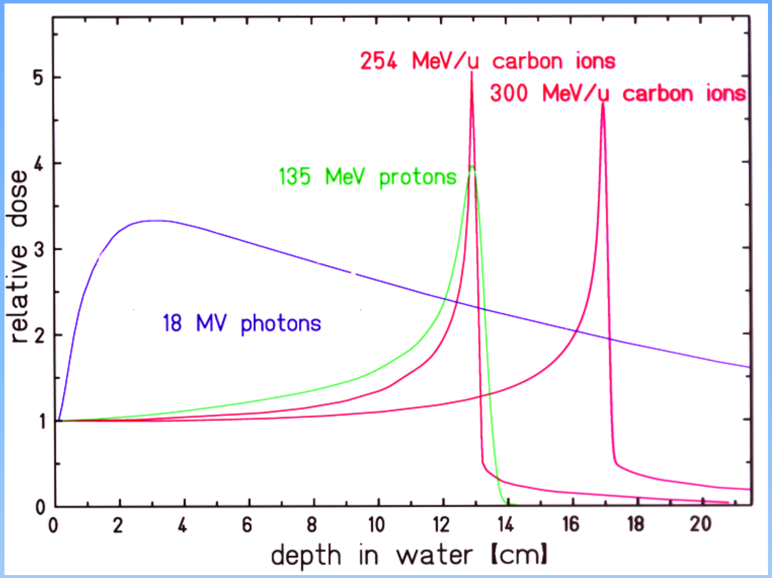


Protons permit to reduce by 2 times dose of normal tissues comparing with x-rays.

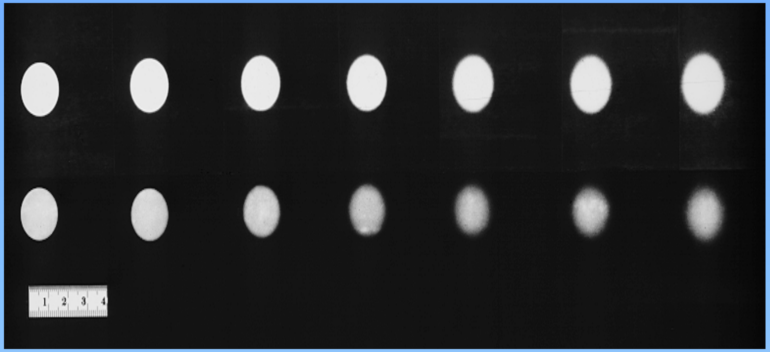
Protons are effectively used at cancer treatment of tumors placed near critical organs.

PROTONS AND CARBON IONS

Depth dose distribution

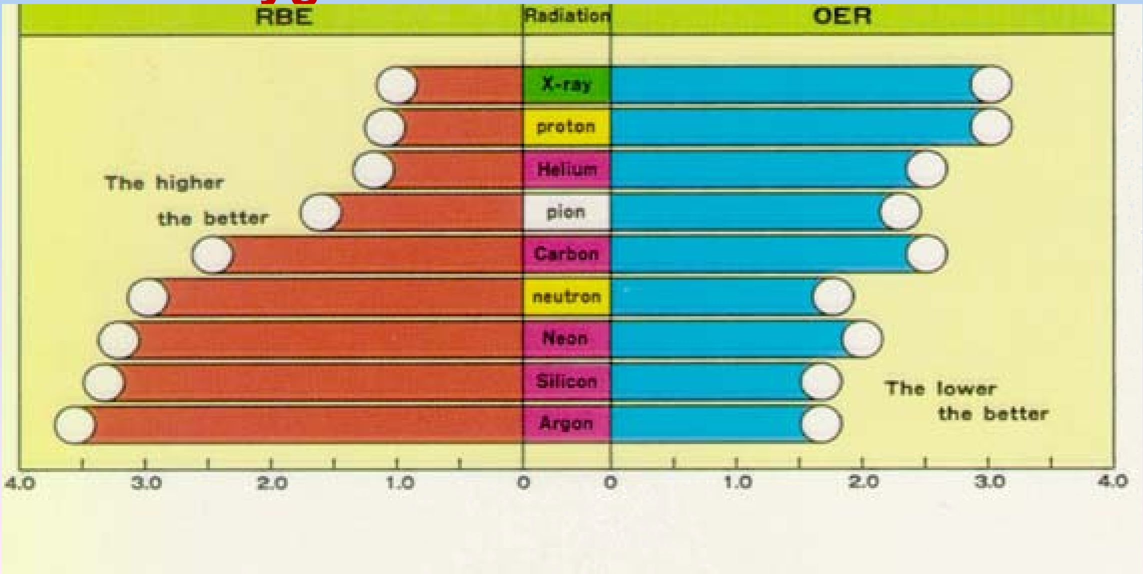


Multiply Scattering



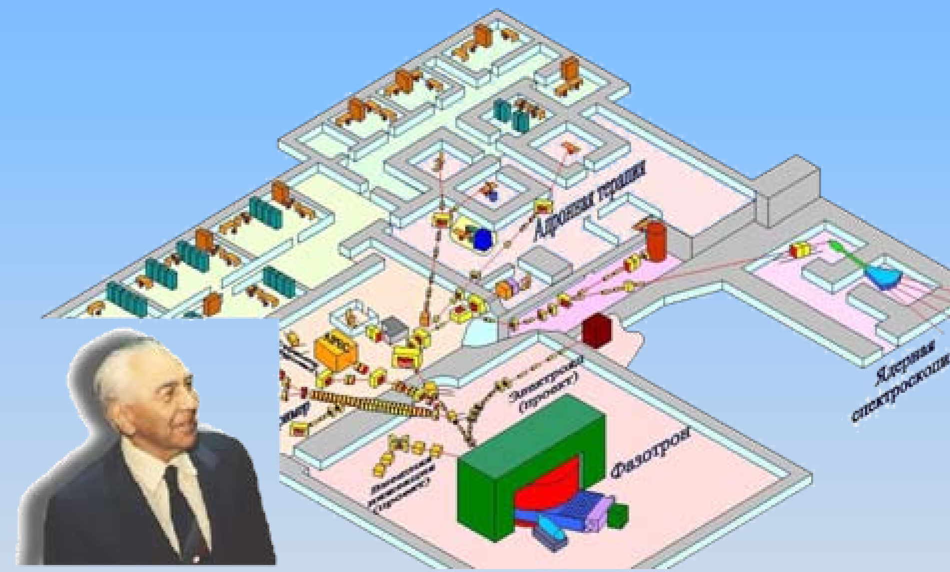
(upper-carbon, down –protons)

Radio Biological Efficiency and Oxygen Enhancement Ratio



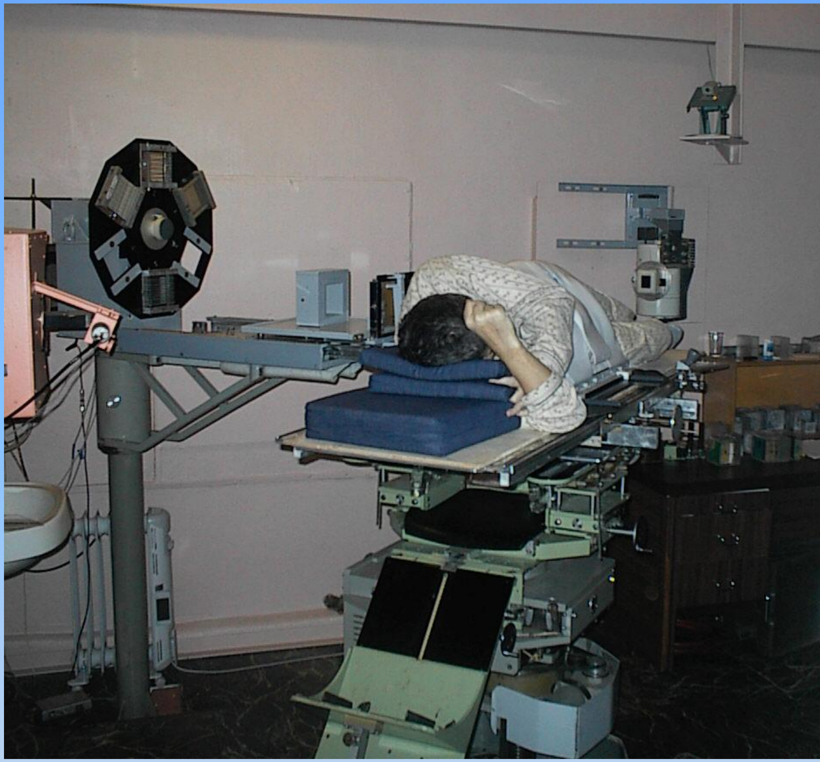
JINR Medical-Technical Complex on proton beams of synchrocyclotron

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 – 2008, – 456 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.

JINR MTC WITH PROTON BEAMS



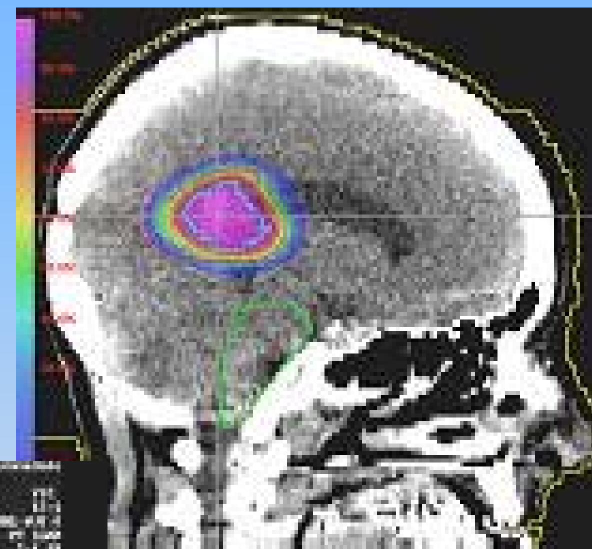
Prostate treatment equipment

Cancer treatment in cabin №1

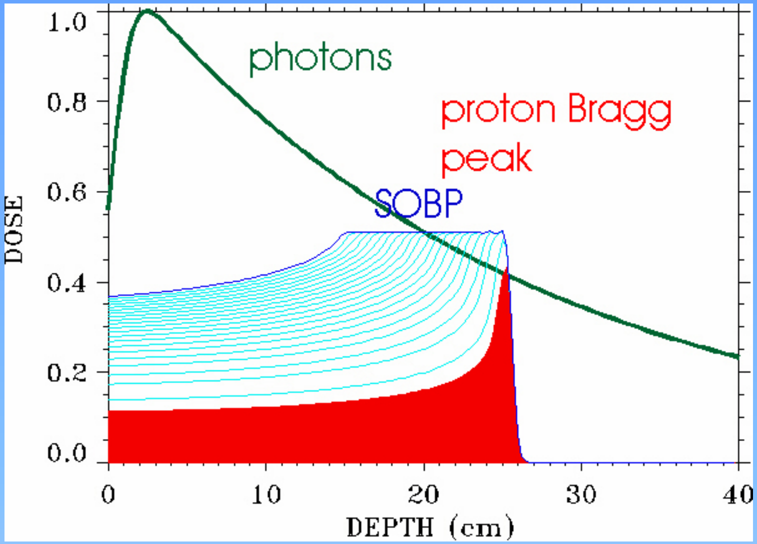
3D conformal proton beam treatment were realized in Russia only in JINR.

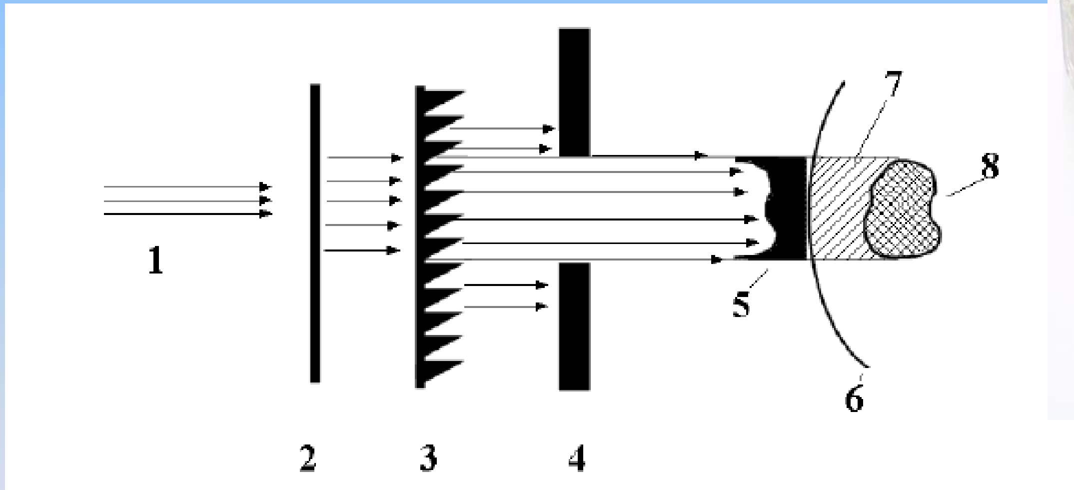
CANCER TREATMENT ON PHASOTRON BEAMS

Plan of proton treatment of brain cancer tissue (right),
NMR tomogram before treatment (left)
NMR tomogram after 3 months later (down)



PASSIVE SPREADING TECHNIQUE

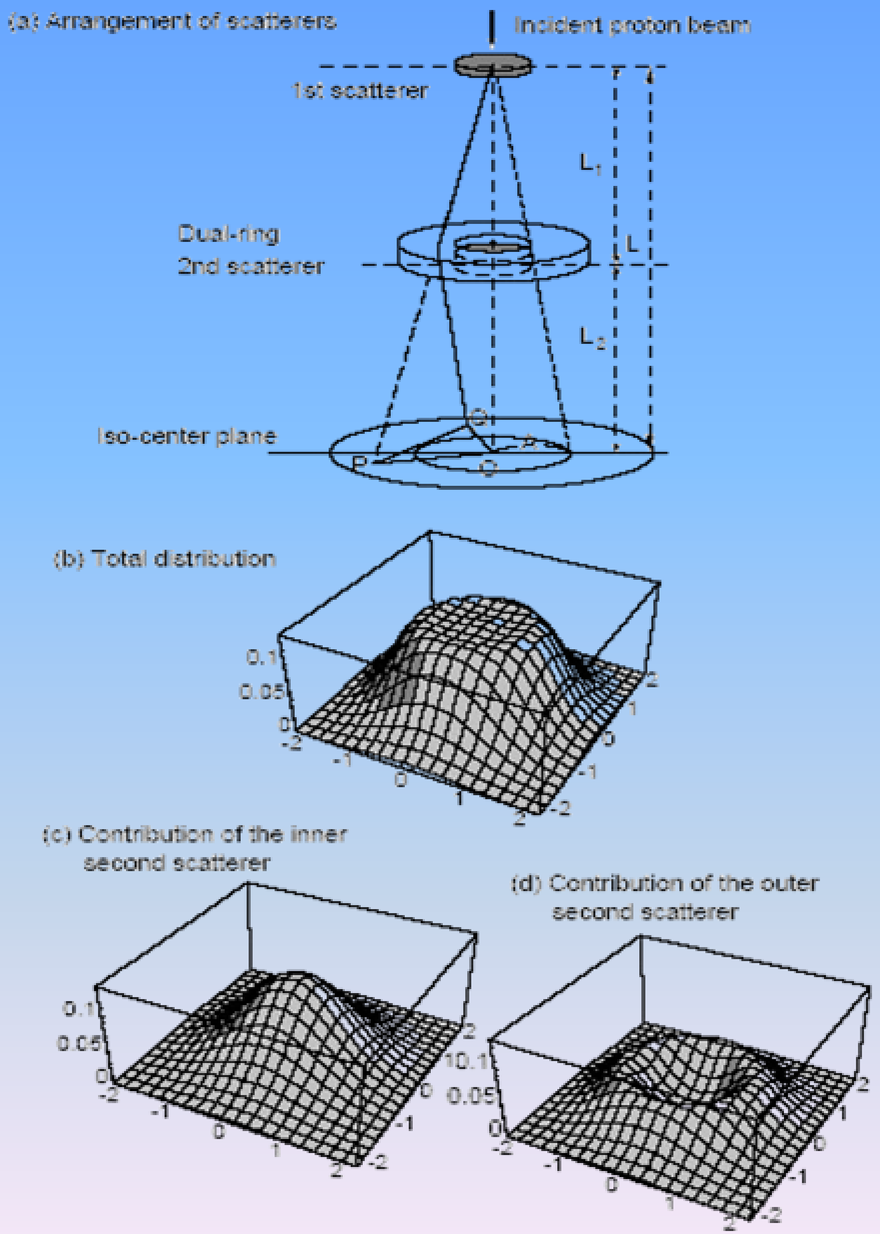




1-proton beam, 2- scattering foil, 3 –ridge filter, 4- collimator, 5 – bolus, 6 – patient surface, 7-dose distribution, 8- tumor target

95 % beam intensity are lost and 5% are utilized for treatment, dose homogeneity is of 4%.

DOUBLE SCATTERING TECHNIQUE



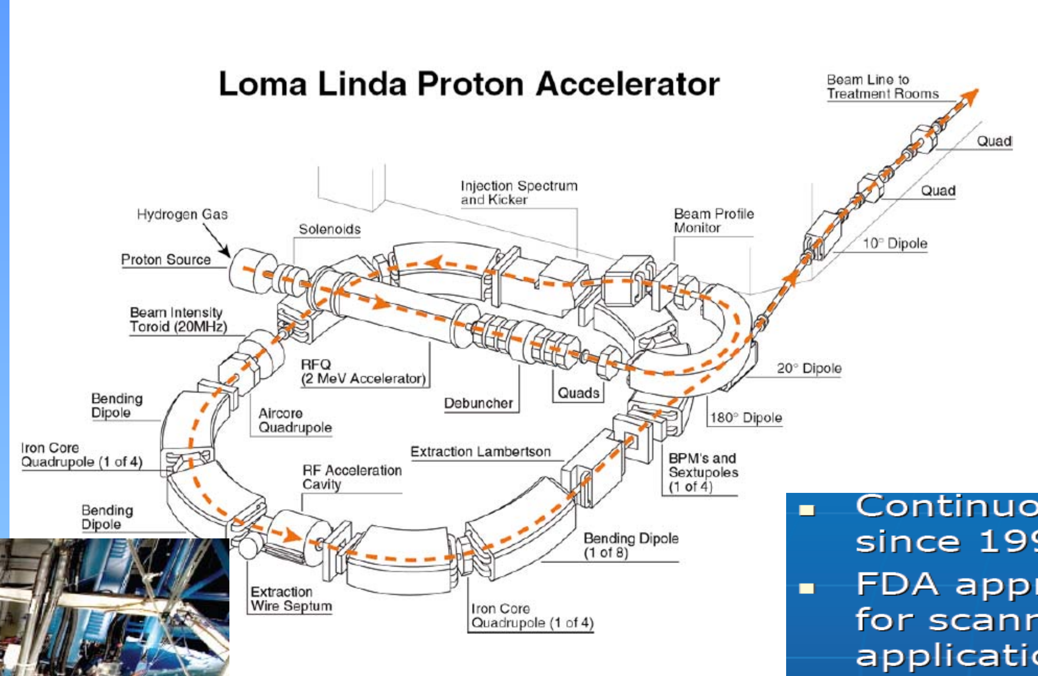
First scatter is a plate
Central part of Second scatter is constructed from a material at Z≈100 (Fig.c), boundary part from material at Z≈6-10 (Fig d).
Homogeneity of dose transverse distribution of ± 2 % (Fig. b)
Efficiency of beam utilization of 30-40 %.

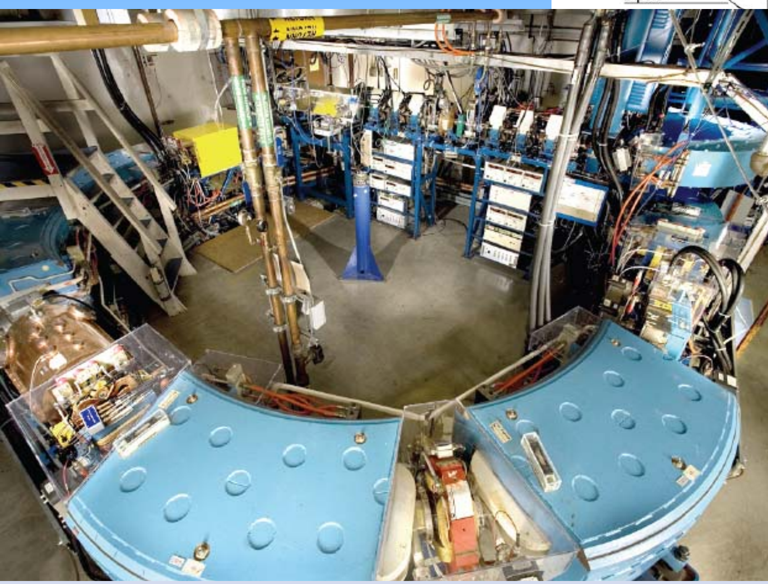
Parameters of proton medical beams

Parameter	Value
Maximal energy, MeV	230-250
Depth of penetration, mm	30
Beam intensity at cancer treatment, p/s	510^9
Maximal dose rate, Gy/l/min	2
Irradiation dose Gy/fraction	2
Number of fractions	20-30
Treatment time, min	2
Homogeneity of irradiation dose, %	±2,5
Maximal tumor volume at passive scanning, l	7,5
Maximal tumor volume at active scanning, l	2
Maximal scanning size on target, cm	20·20
Spot size of pencil beam, mm	3

Parameters of medical proton cyclotrons and synchrotrons

Parameter	Cyclotron	Synchrotron
Energy of extracted particles	**fixed**	**variable**
Energy variation rate, MeV/s	**15**	**4**
Energy spread, %	**0,5**	**0,1**
Stability of energy, %	**0,1**	**0,1**
Maximal beam current, nA	**300**	**15**
Current modulation time, ms	**1**	**1**
Extraction efficiency, %	**60-80**	**90**
Beam utilization, %	**50**	**>50**
Working cycle, %	**100**	**70**
Emittance of extracted beam, $\pi \cdot$mm$\cdot$mrad	**5**	**2-3**
Diameter of accelerator, m	**4-5**	**7-8**
Weight, t	**200-250**	**20-30**



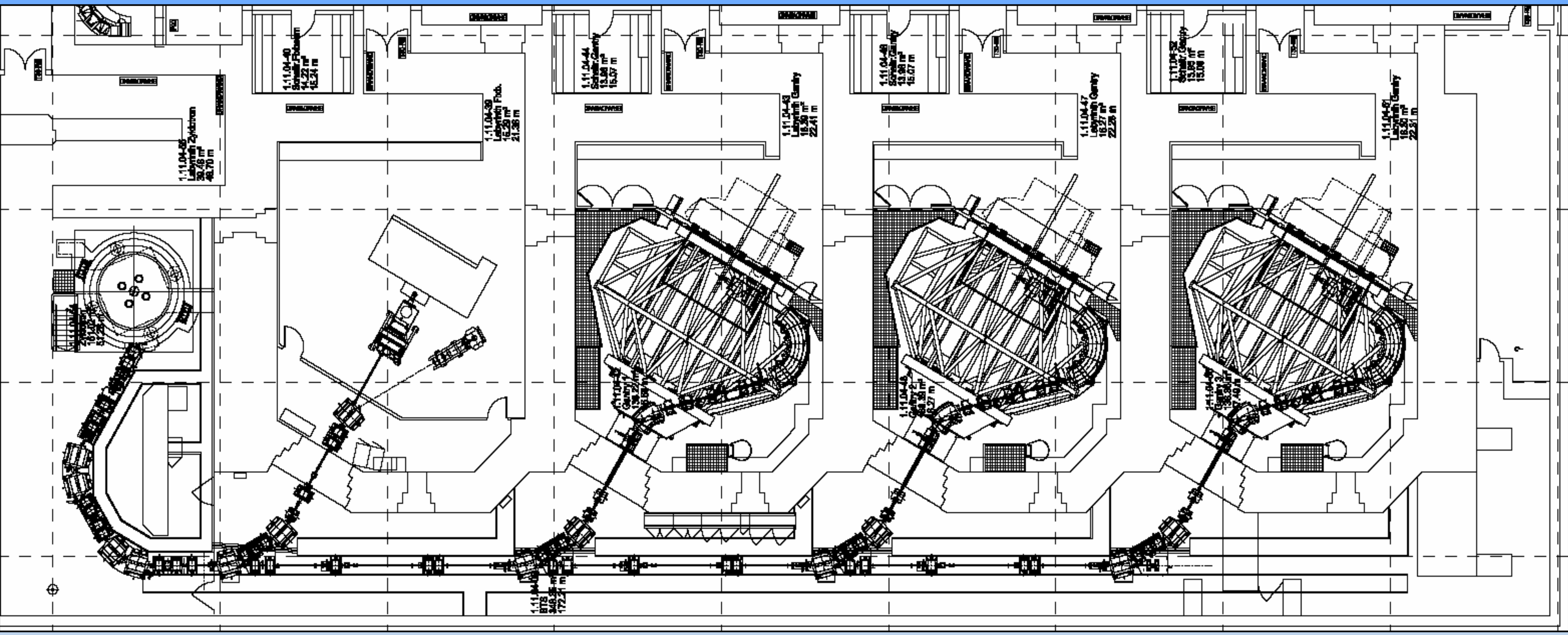


- Continuous operation since 1990
- FDA approved (also for scanning applications)
- 98% reliability with 24/6 operations
- 2 Gy/min for volume of 1 liter, field size = 13 cm dia.
- Proton range stability 0.1 mm
- New control system in 2002 for beam scanning upgrade
- Uses slow extraction

Hospital synchrotron centers of proton therapy Hitachi (3 clinical centers), Mitsubishi (1 clinical center and vendor for 6 facilities at Japan), Optivus Tech. Inc. (1 clinical center).

Hospital cyclotron centers of proton therapy IBA (6 clinical centers and 5 projects is under realization), Accel (2 clinical centers).

IBA CYCLOTRON CENTER OF PROTON THERAPY

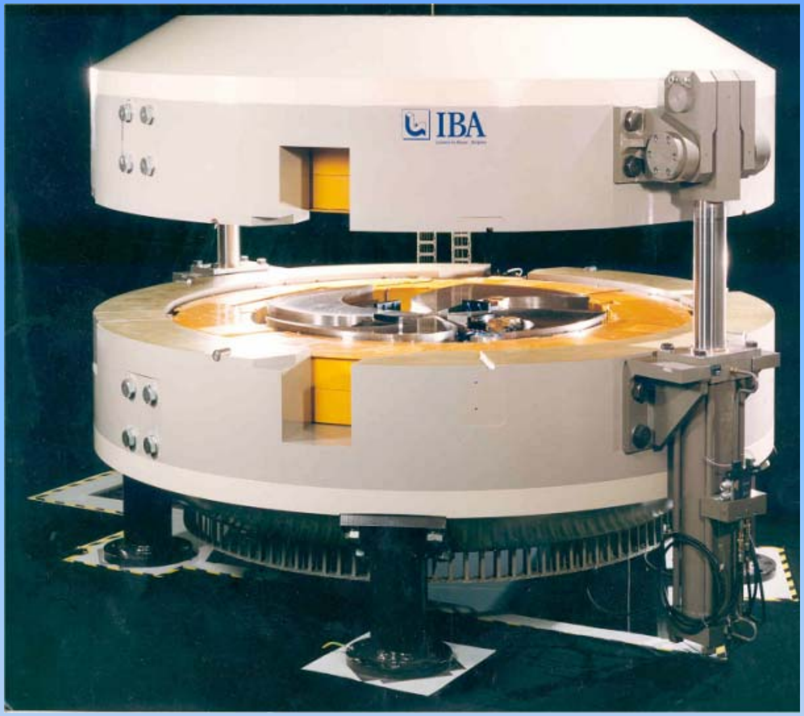


There are 22 centers of the proton therapy at the world now. More than 47.5 thousand patients were treated with application of proton therapy during last 50 years,

60 % of them were treated over last 10 years and 90% of total patients now treated in the hospital based facilities.

MEDICAL PROTON CYCLOTRONS

New PSI superconducting cyclotron at 250 MeV



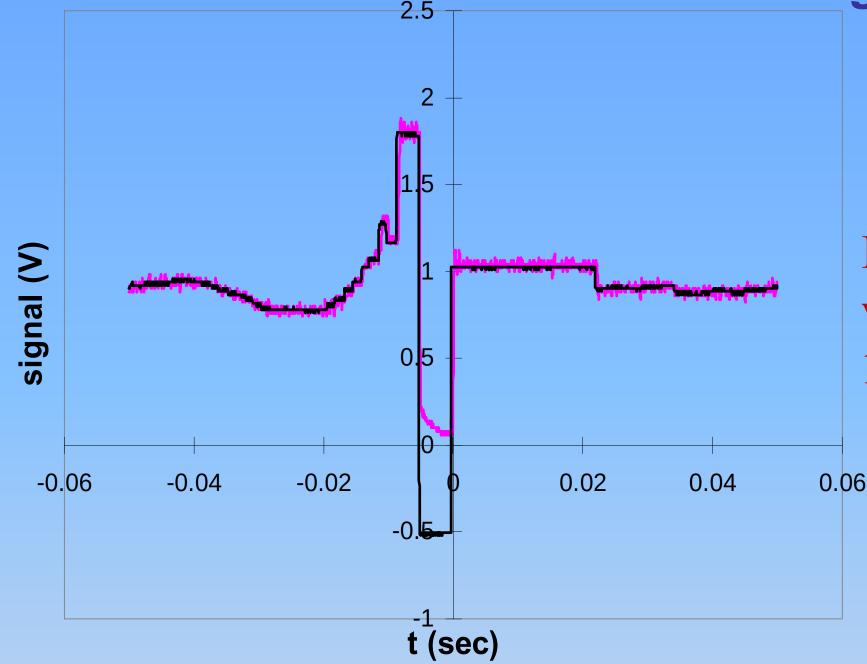
IBA proton cyclotron

Advantages:

simplicity,
reliability,
lower size,
ability to modulate rapidly and accurately the beam current.

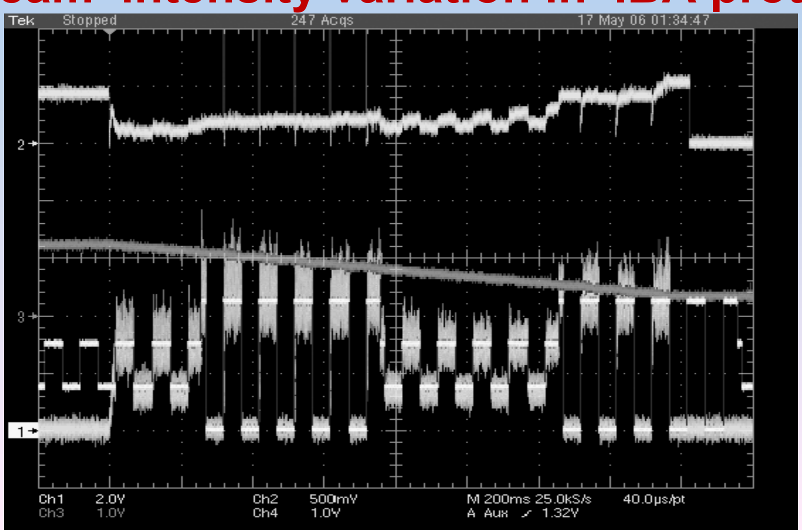
BEAM CURRENT MODULATION

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

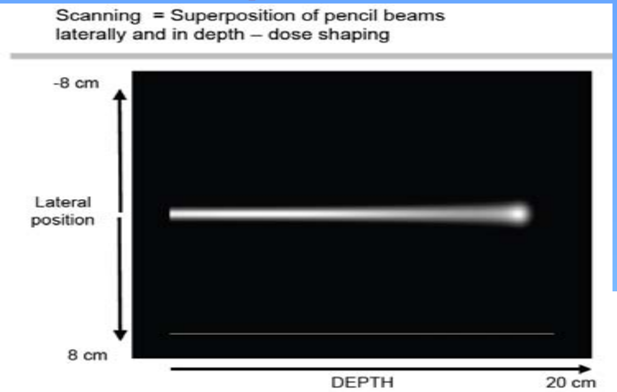
Parameters of proton isochronous cyclotron C235

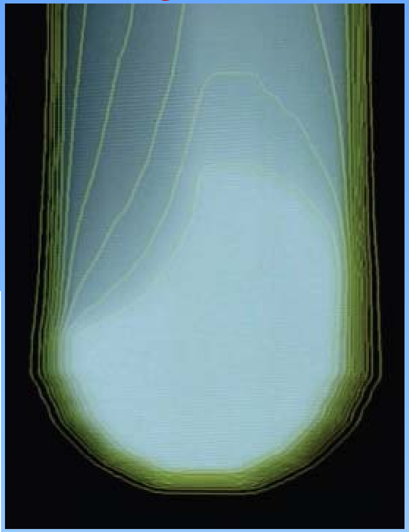
General parameters	Value
Proton energy, MeV	235
Internal current, nA	300
Beam emittances, π·mm·mrad	12/11
Magnetic field (min/max) T	0.9/2.9
Number of sectors	4
Magnet diameter, m	4.3
Radius of beam extraction, m	1,08
Elliptical hill gap, cm	9,6/0,9
Duant aperture, cm	2
RF frequency, MHz	106.1 (4 harmonic)
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

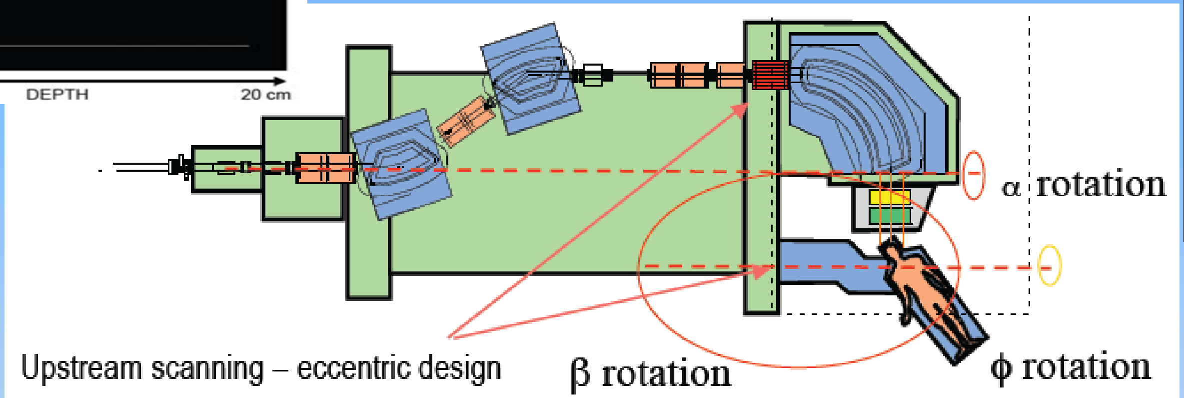
ACTIVE PENCIL BEAM SCANING

Active Spot Pencil Beam Scanning technique was developed in PSI cyclotron center of proton therapy

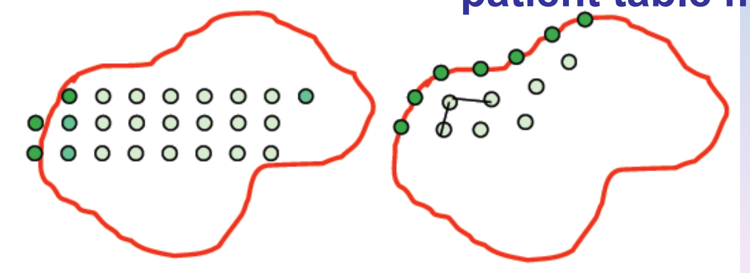
σ=3mm , grid step=5 mm



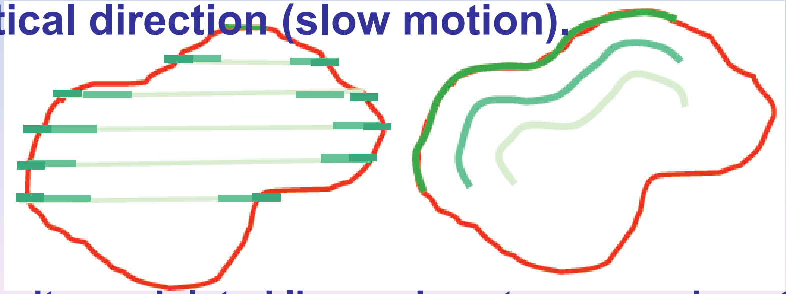




PBS scanning:
fast kicker in time;
range shifter in z-direction;
sweeping magnet in horizontal direction;
patient table motion in vertical direction (slow motion).



Spot scanning at gantry 1



Intensity modulated line and contour scanning at gantry2

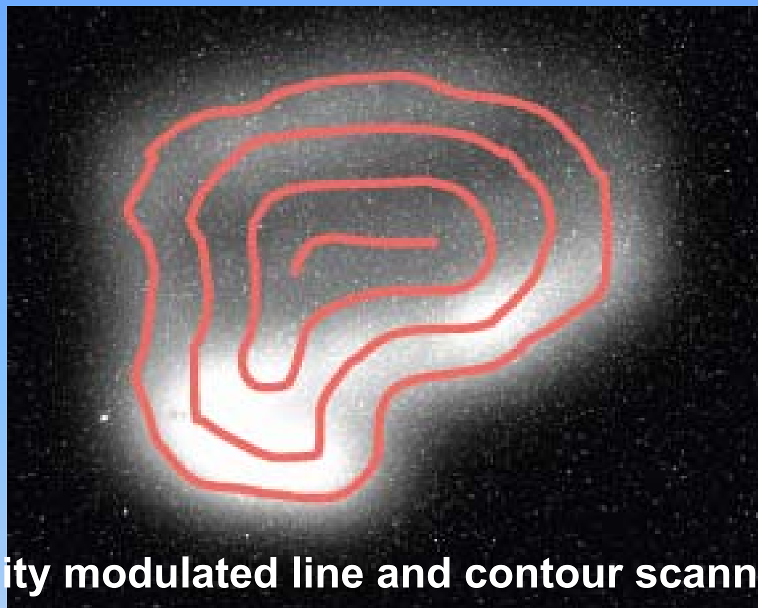
Present PSI active beam scanning system

Sweeper magnets – 3 ms for 5 mm step
Range shifter -40 plates (dead time 50 ms, 30 ms motion)
Patient table –step motion of 5 mm, 1 s dead time per step
(Slow motion-impossible to repeat repainting)

Parameters of PSI active spot treatment

Tumor volume – 1 liter (max 4 liters)
Beam size, σ=3mm
Grid step, 5 mm
Number of spots 21 lateral- 23 depth
$21 \cdot 21 \cdot 23 \approx 10\,000$ spots/liter
Beam-ON treatment time -1.5 min
Average 10 ms/spot
Required intensity – 0.2 nA for
1min-1Gy-1 liter
Dead time-1.5 min=
sweeper ($10\,000 \cdot 3$ms)+table($21 \cdot 1$s)+shifter($21 \cdot 21 \cdot 50$ ms)
Duty factor -50%

Planed PSI IMPT
at active PBS with gantry 2



Intensity modulated line and contour scanning

Rotation from -30 to +180 degrees

IMPT

Painting of contours -1 cm/ms (10 ms per line 10 cm)

Beam intensity modulation -0.1 ms

Painting of an energy iso-layer -200 ms/plane (20 lines·5 mm)

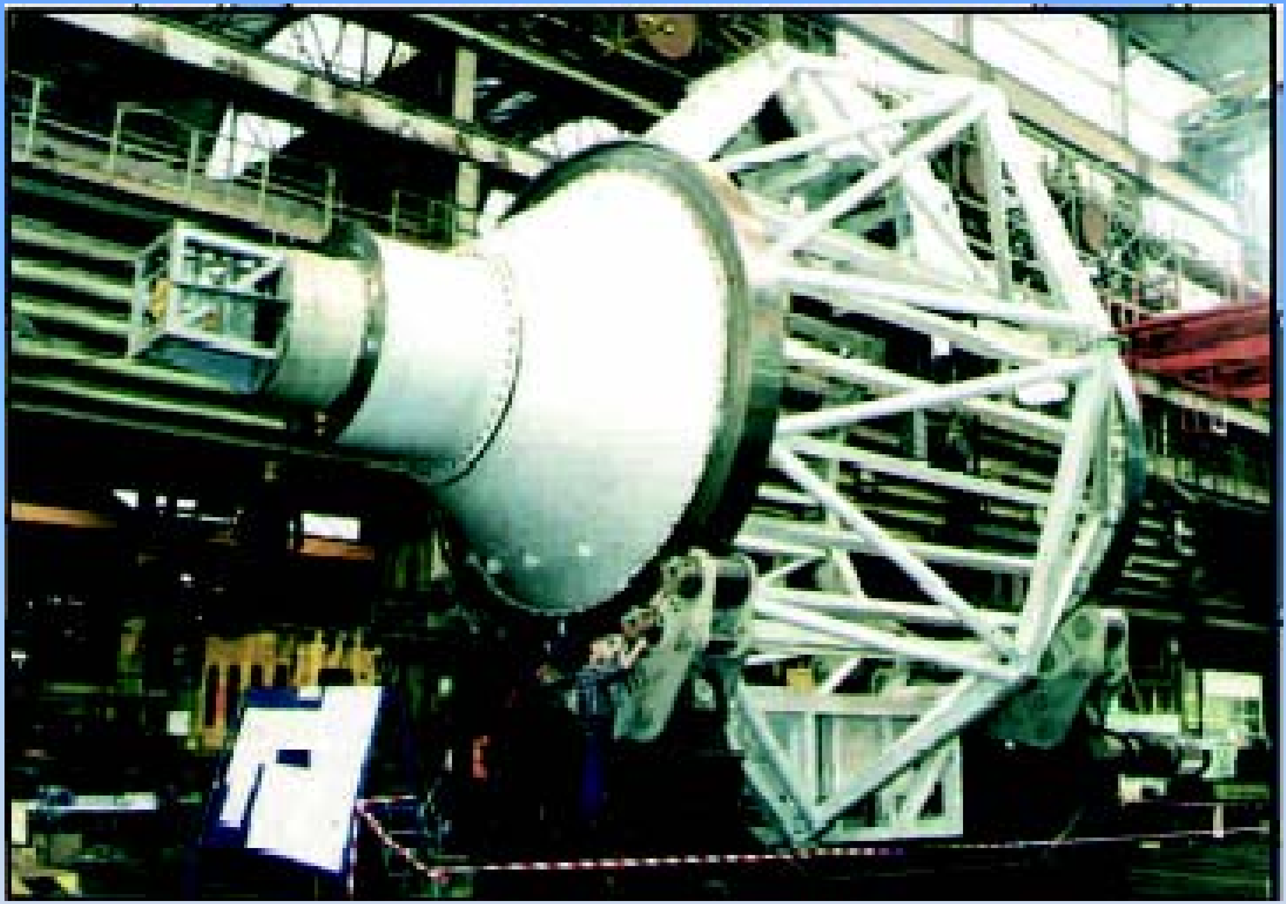
Change of energy 100 ms- 5 mm range

(by wedge degrader and beam line, it is one order higher than in synchrotron)

Painting of volume- 6s/1 liter (20 energy steps of 5 mm)

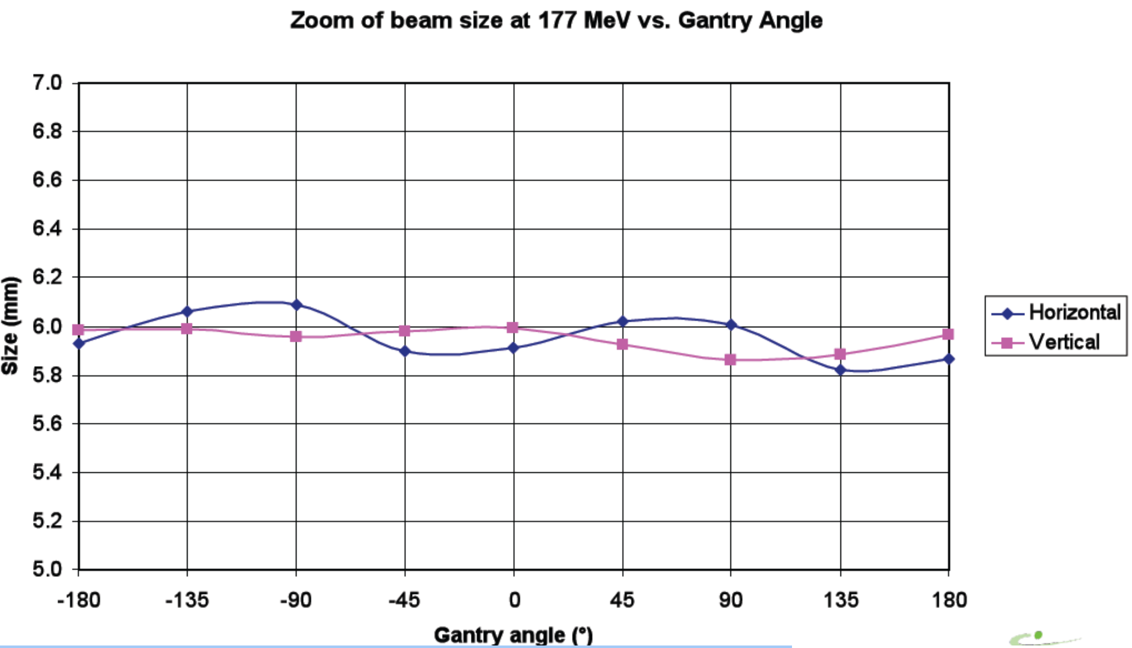
Volumetric repainting-10-20 repainting/1 liter at 1-2 min.

Gantry system

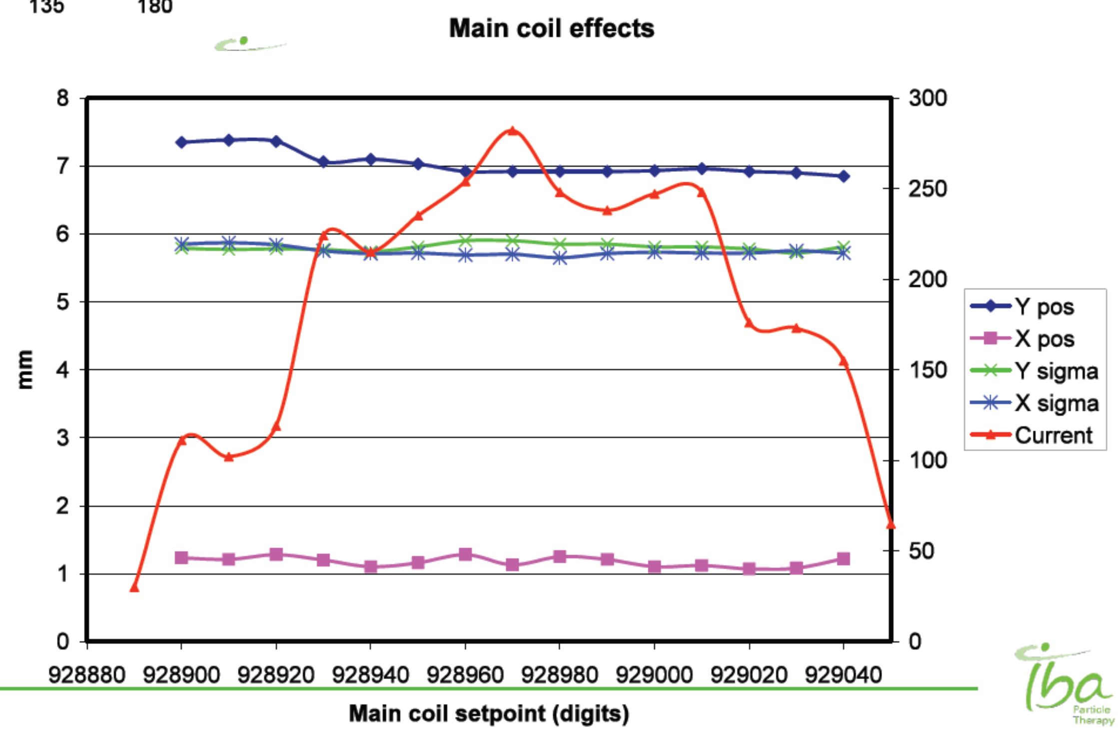


IBA proton gantry,
weight about 100 t, diameter > 6 m
Proton beam displacement from isocenter <1 mm
In Center with out gantry proton therapy is recommended for 7% of tumor patients, with gantry-30%.

Cyclotron beam size at IBA gantry isocenter

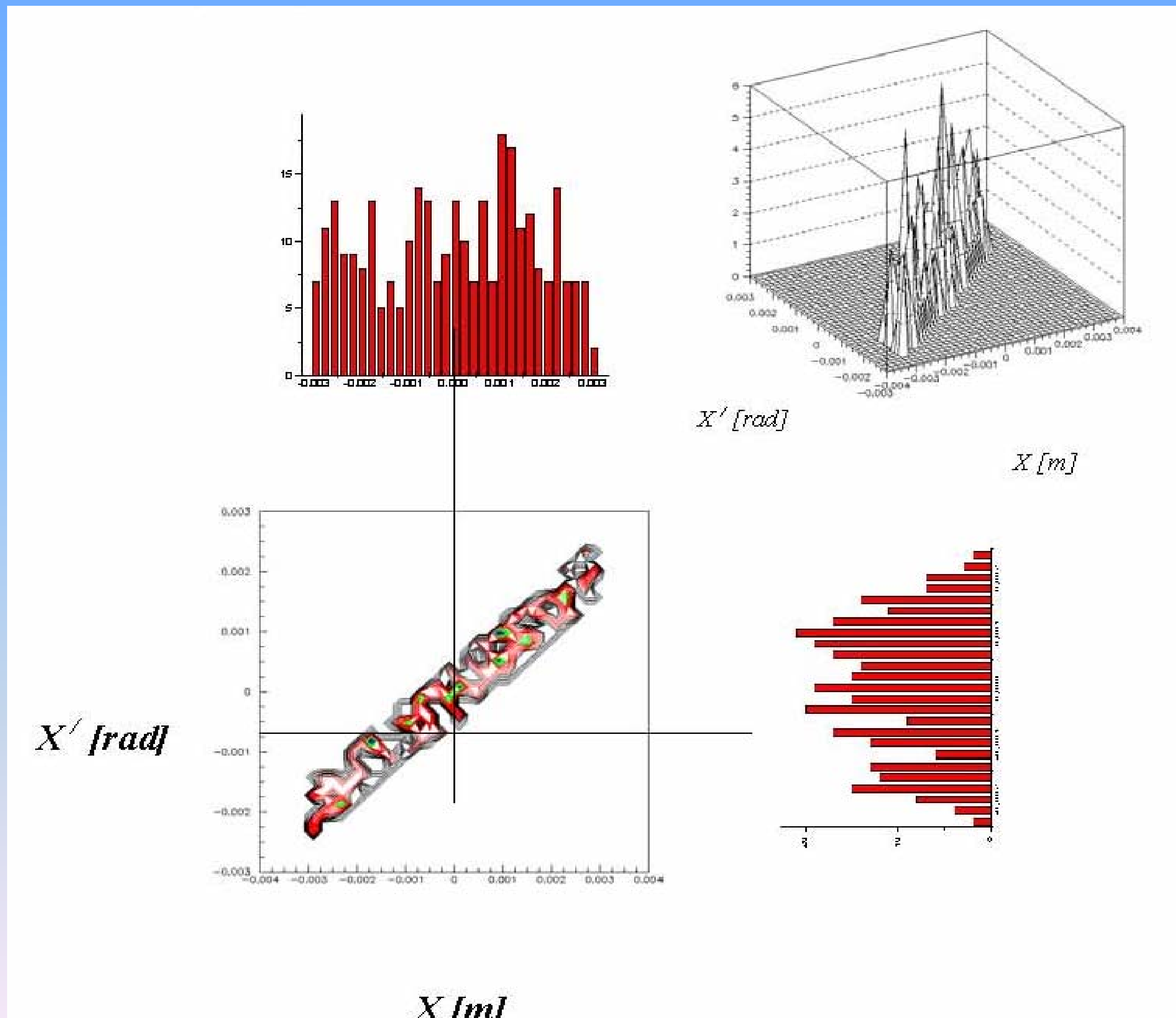


Cyclotron tuning



Non Gausian distribution in horizontal phase space of extracted synchrotron proton beam

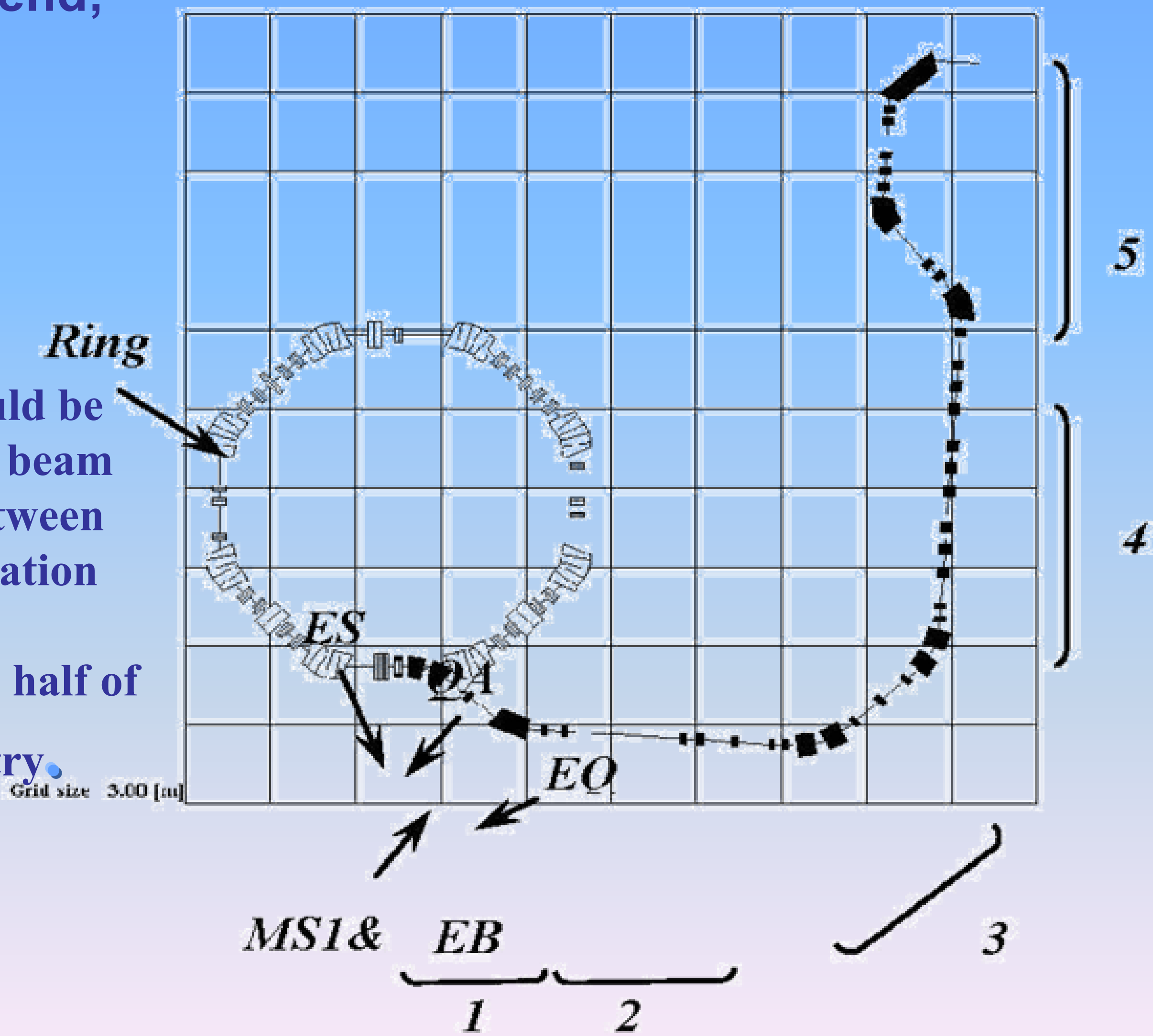
Horizontal phase-plane



There are correlation between the horizontal profile and gantry rotation angle.

General layout of the synchrotron extraction beam line

1)matching section between the ring and the extraction beamline
2)a 'chopper' region;
3)a zero-dispersion bend;
4) 'rotator' section;
5)a 'gantry' section.

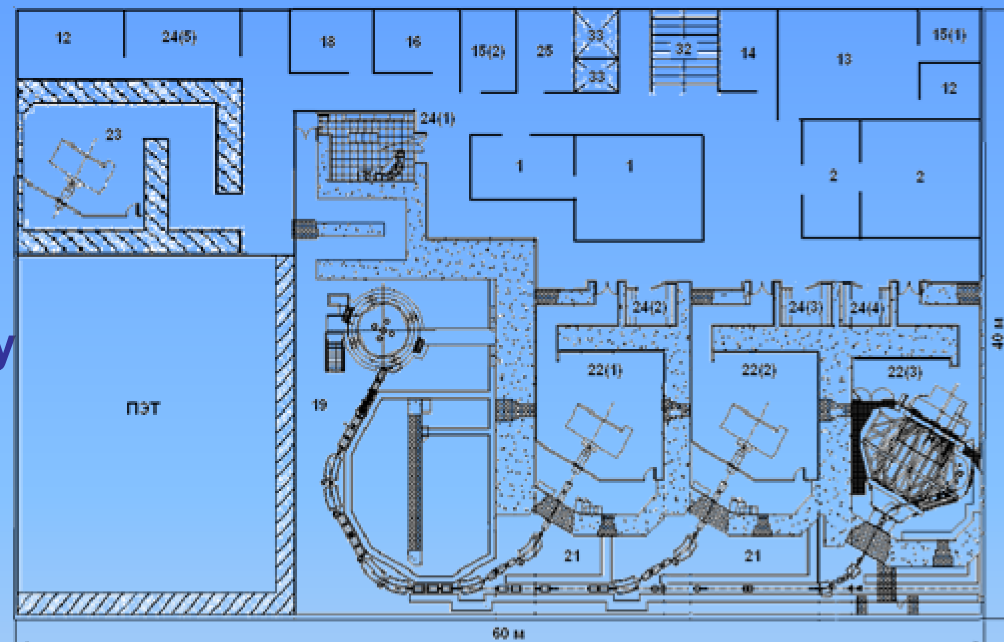


Special rotator section should be installed in the synchrotron beam line to avoid correlation between beam shape and gantry rotation angles .
This section rotates beam on half of rotation angle of the gantry.

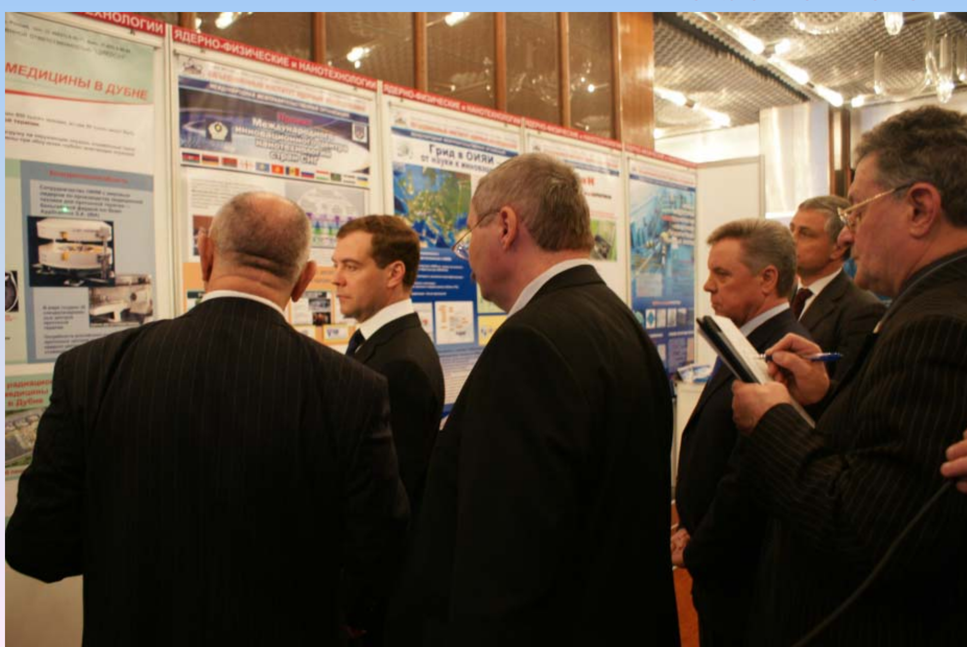
DUBNA CYCLOTRON CENTER OF PROTON THERAPY

Dubna Center of Radiation Medicine (CRM) involves:

Cyclotron Center of Proton Therapy,
PET center,
Department of convention radiotherapy with electron linac,
Diagnostic department,
Proton therapy clinic.



The scheme of accelerator equipment of Dubna CRM.



The Center of proton therapy has 3 treatment cabins, 1 with the gantry and 2 rooms with the fixed beams.

About 1000 patients per year will be treated there.

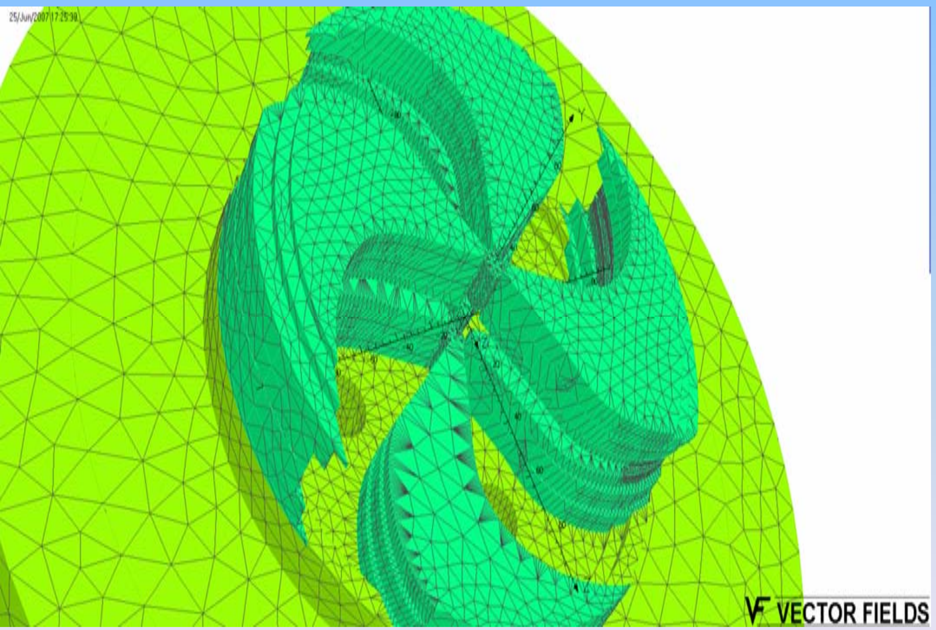
Modified Cyclotron C235

JINR-IBA collaboration develops a medical cyclotron for the proton therapy.

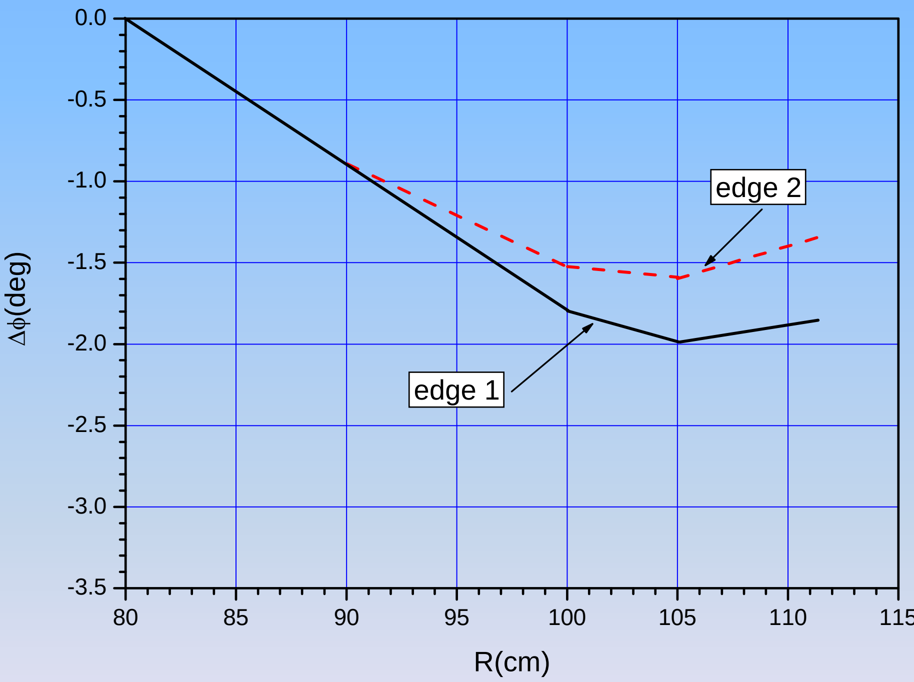
This year it is planned to complete its construction and in 2009 to carry out the beam tests.

After that the accelerator could be installed in the Dubna hospital Centre of proton therapy.

The main modernization efforts are directed on optimization of the magnetic system oriented on an increase of the axial betatron frequency.

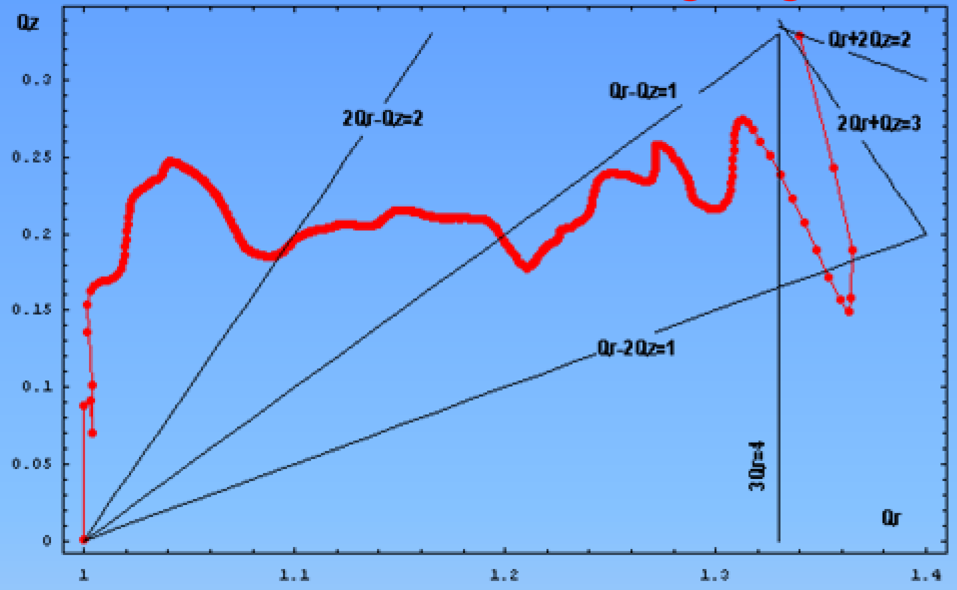


Simulation of magnetic field.

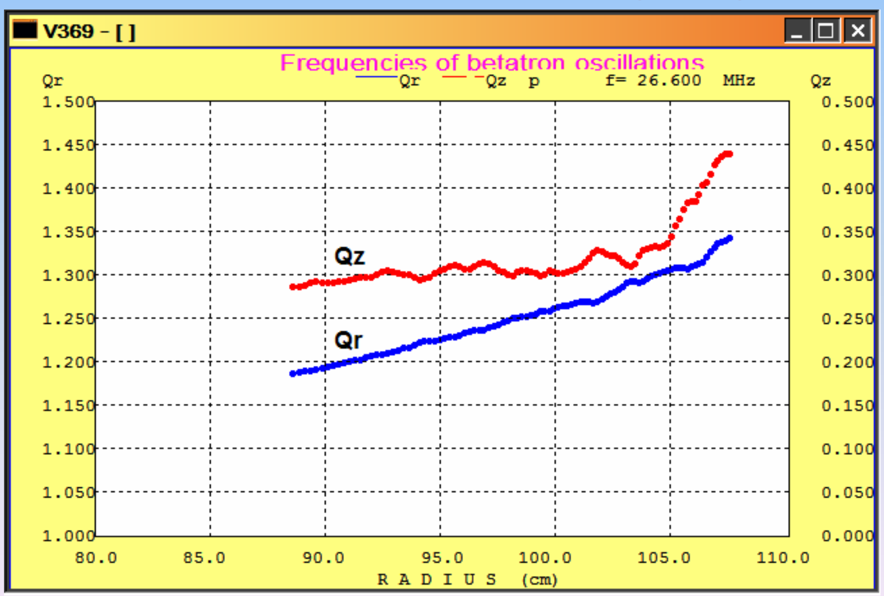


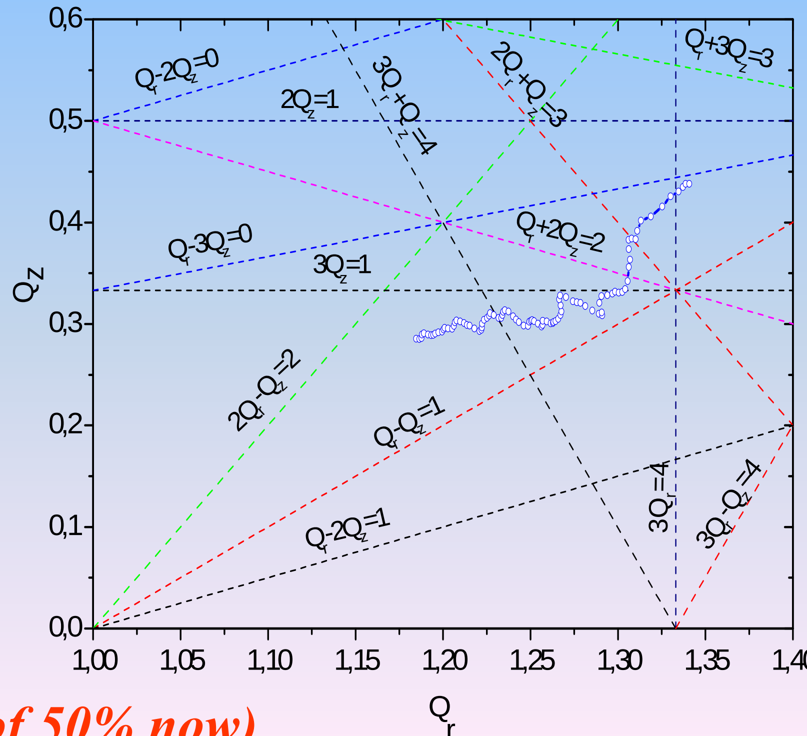
Azimuthal angle variation

C235 working diagram



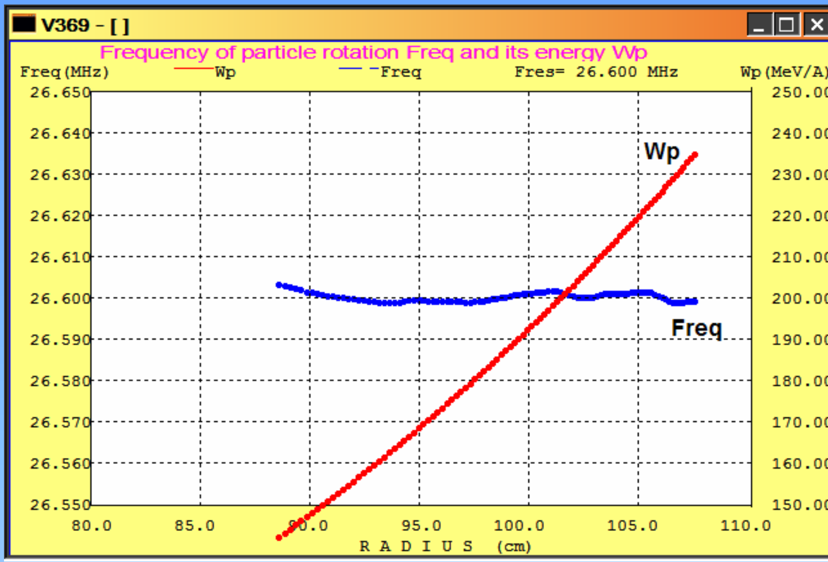
Modified C235 New working diagram



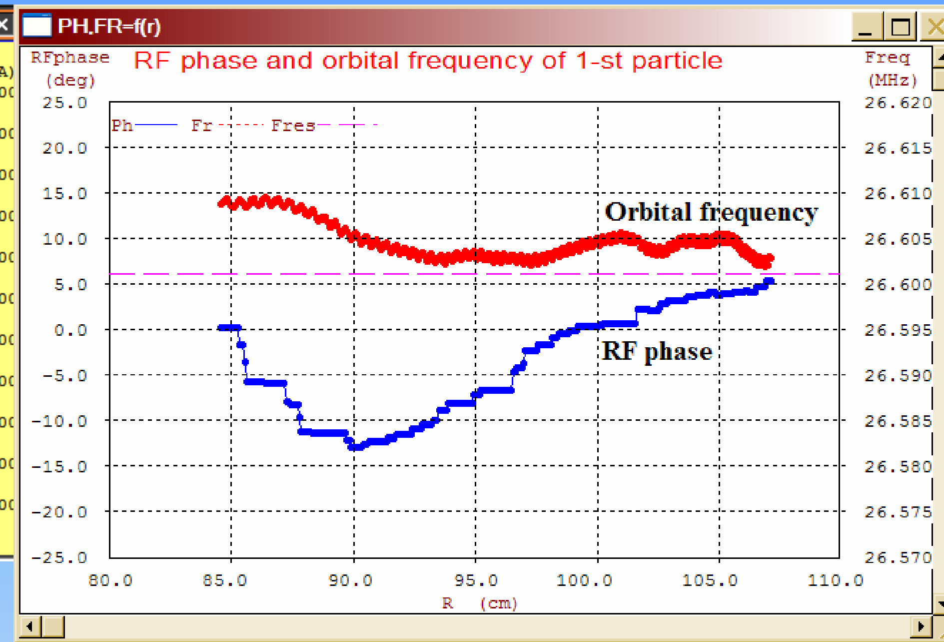


To provide small internal losses (<15% instead of 50% now)

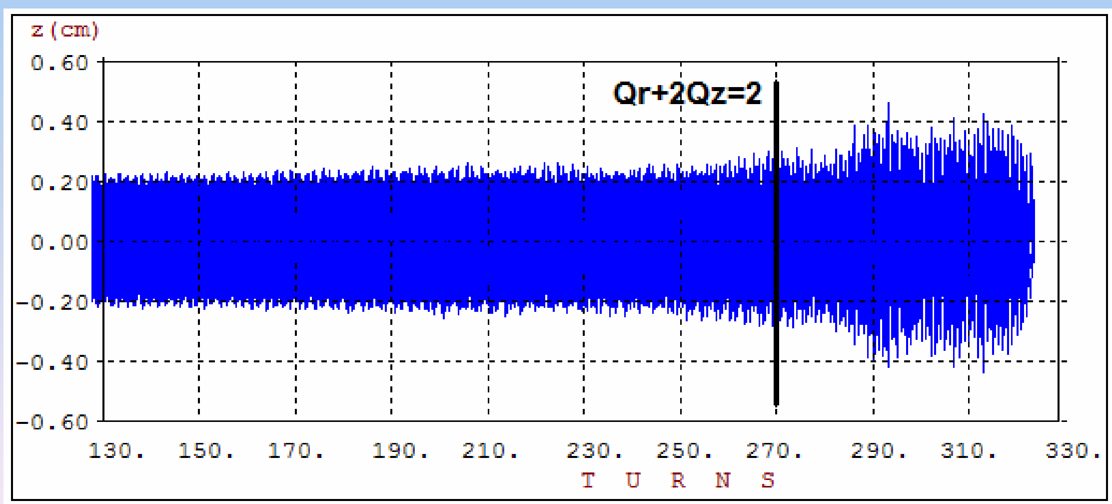
Proton acceleration in modified C235



Dependence of proton orbital frequency and energy on radius

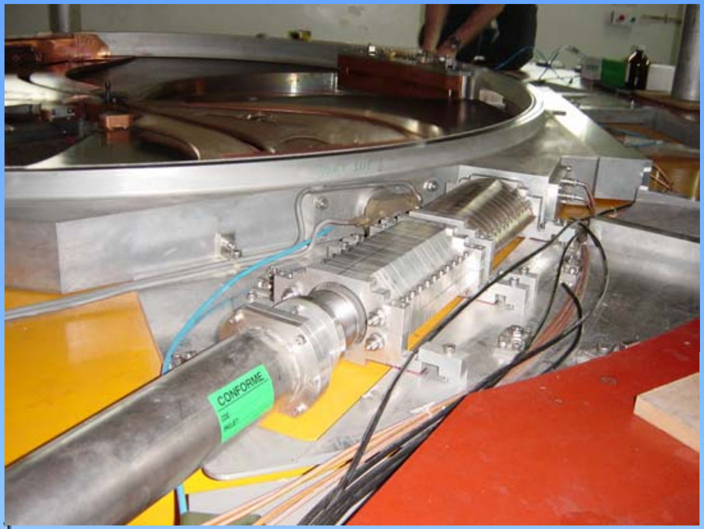


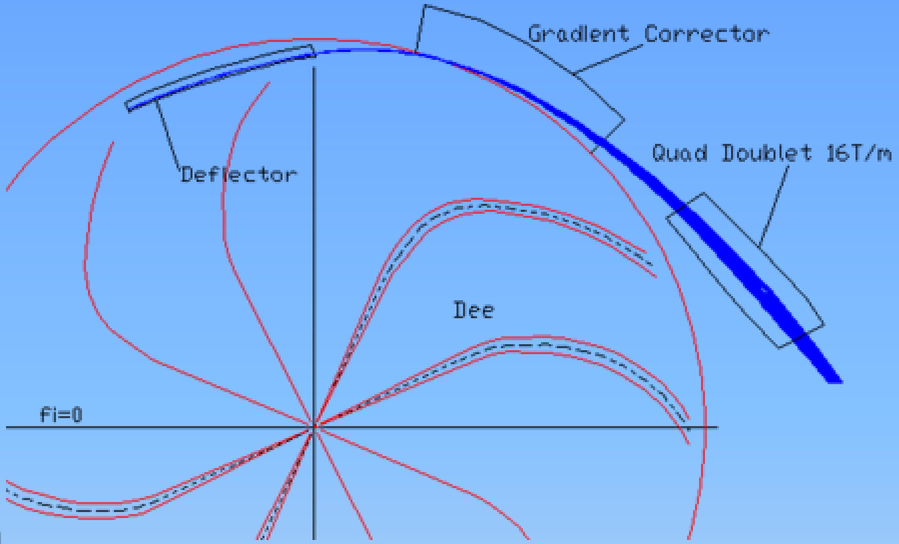
Phase motion of equilibrium particle

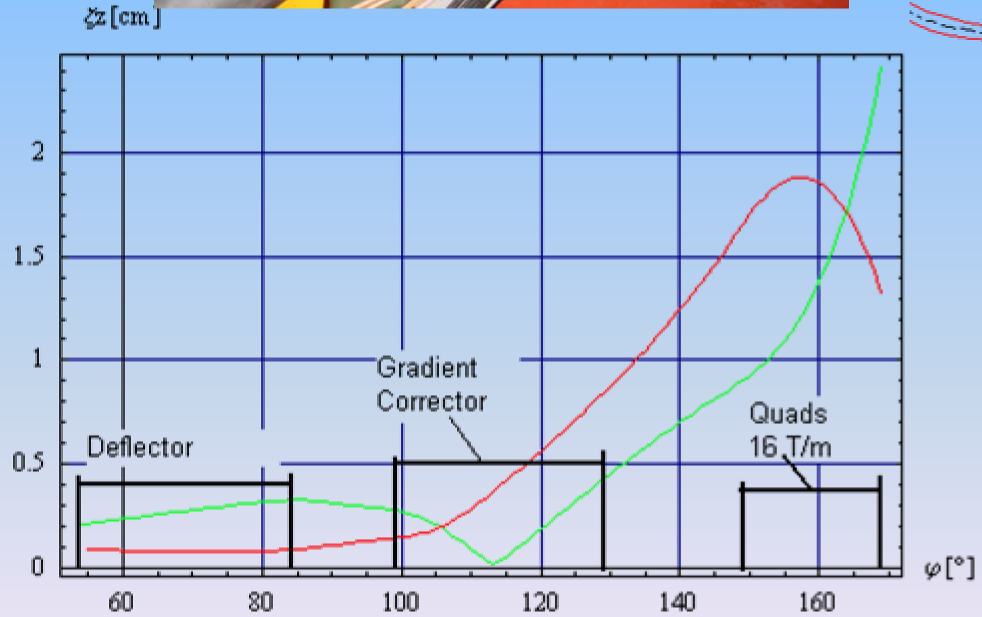


Axial proton motion (4 points per turn) at A_r=4 mm.

Modified C235 Beam extraction simulations



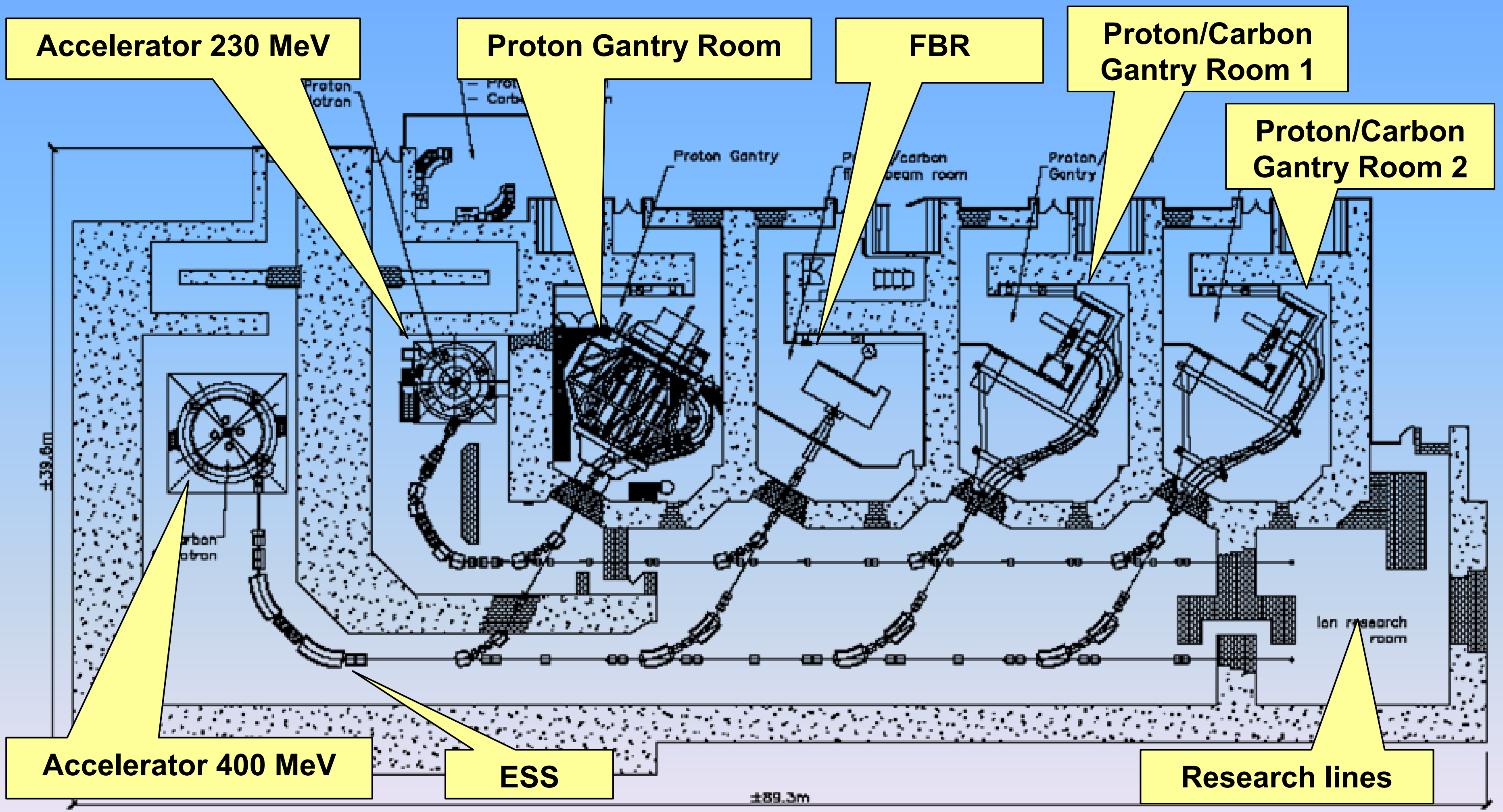




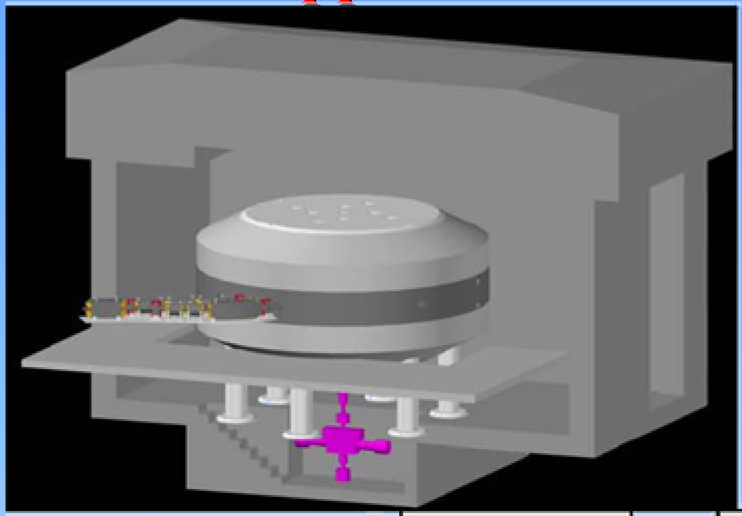
r.m.s-sizes of extracted proton beam

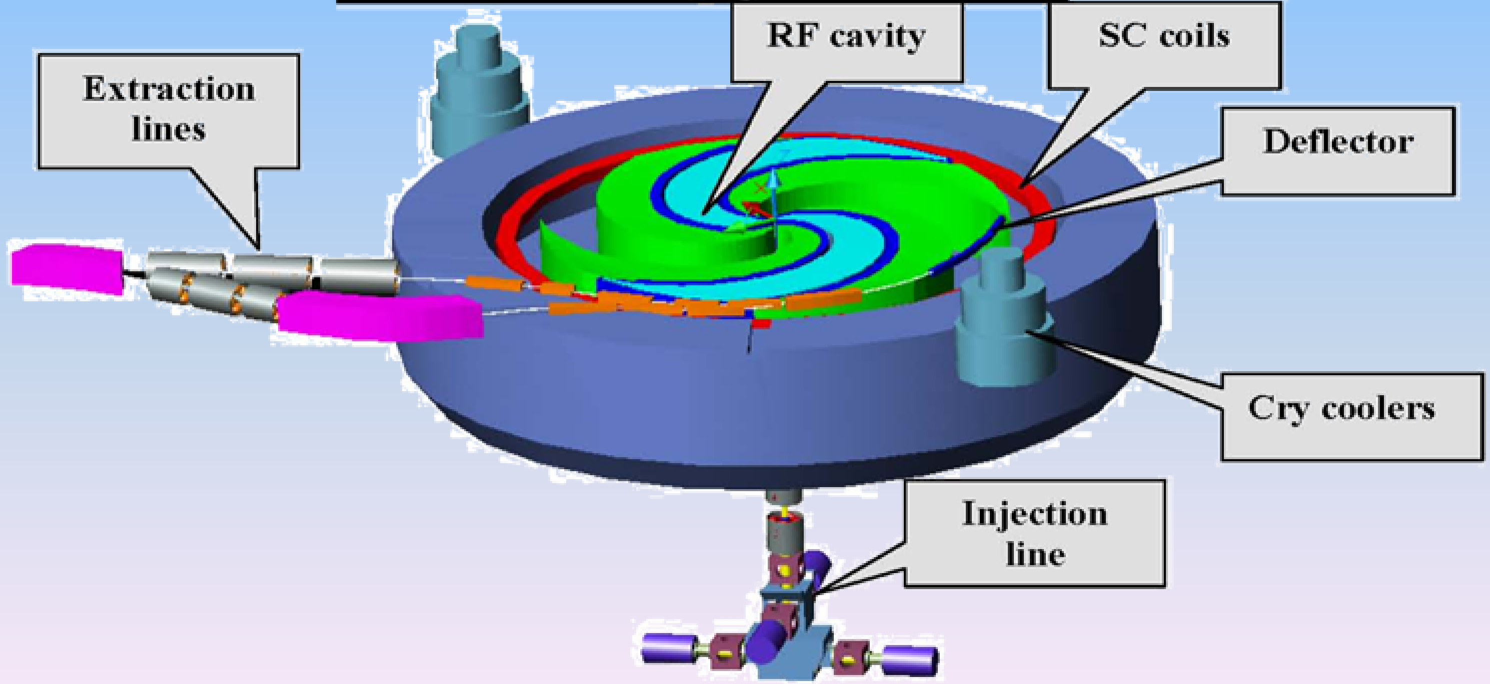
Simulation extraction efficiency is ~71.4% - at amplitude of radial oscillation of 4 мм.

The IBA proton-carbon facility



JINR-IBA C400 Design applied for carbon therapy





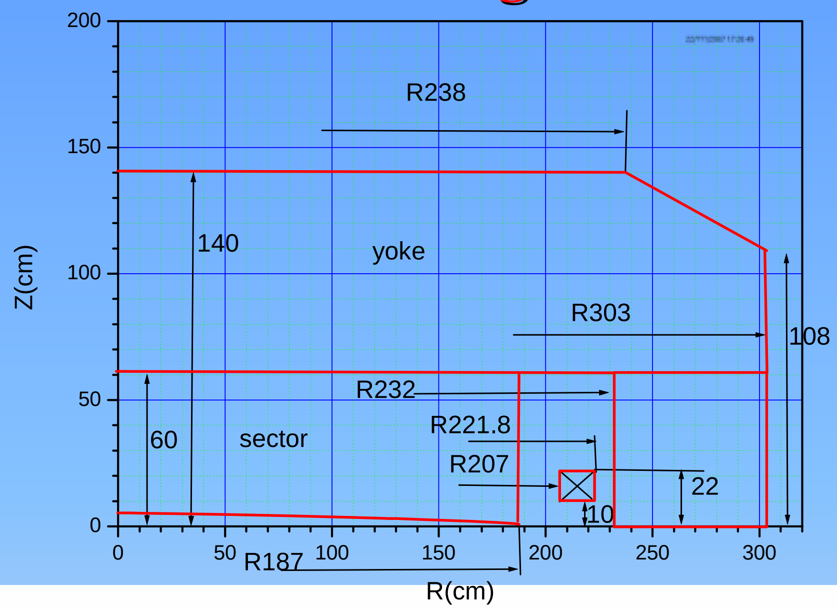
Parameters of the C400 cyclotron

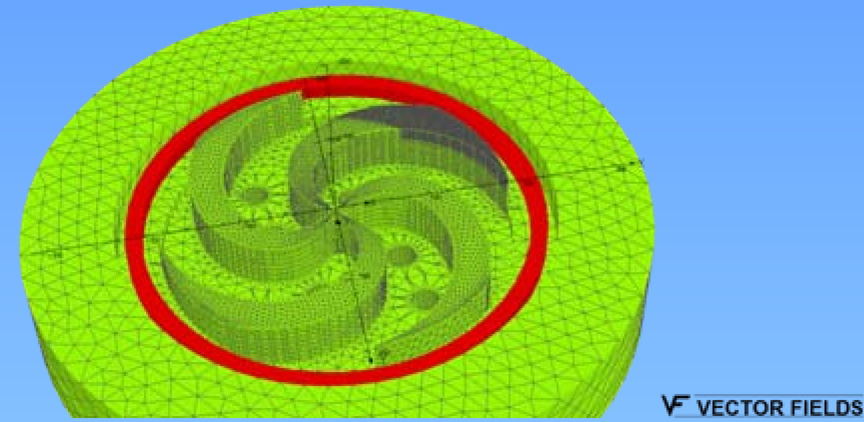
General properties	
accelerated particles	H_2^+, $^4He^{2+}$, ($^6Li^{3+}$), ($^{10}B^{5+}$), $^{12}C^{6+}$
Injection energy	25 keV/Z
final energy of ions, protons	400 MeV/amu 265 MeV/amu
extraction efficiency	70 % (by deflector)
number of turns	~1700
Magnetic system	
total weight	700 tons
outer diameter	6.6 m
height	3.4 m
Pole radius	1.87 m
valley depth	60 cm
bending limit	K = 1600
hill field	4.5 T
valley field	2.45 T
RF system	
radial dimension	187 cm
vertical dimension	116 cm
Frequency	75 MHz
Operation	4th harmonic
number of dees	2
dee voltage:center/extraction	80/170 kV

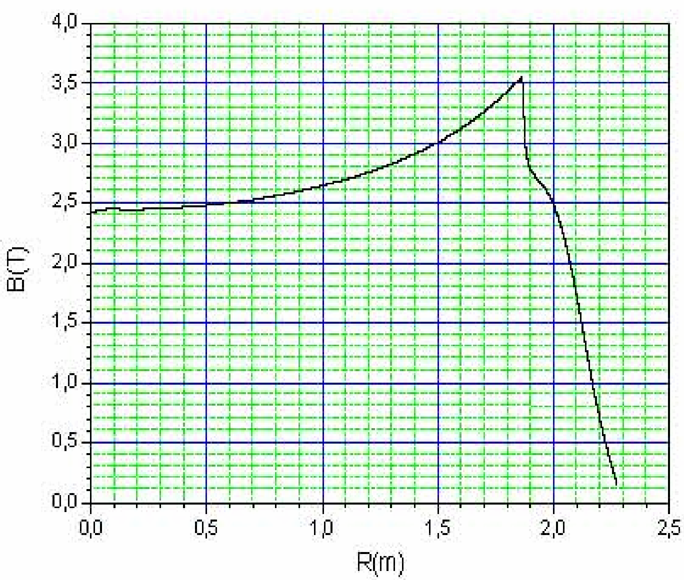
Cyclotron efficiencies and currents

	Goal	
Source	3000	enA
Axial injection	90.00%	
Central region	25.00%	
Acceleration	90.00%	
Extraction	65.00%	
Total efficiency	13.16%	
Extracted current	394.9	enA

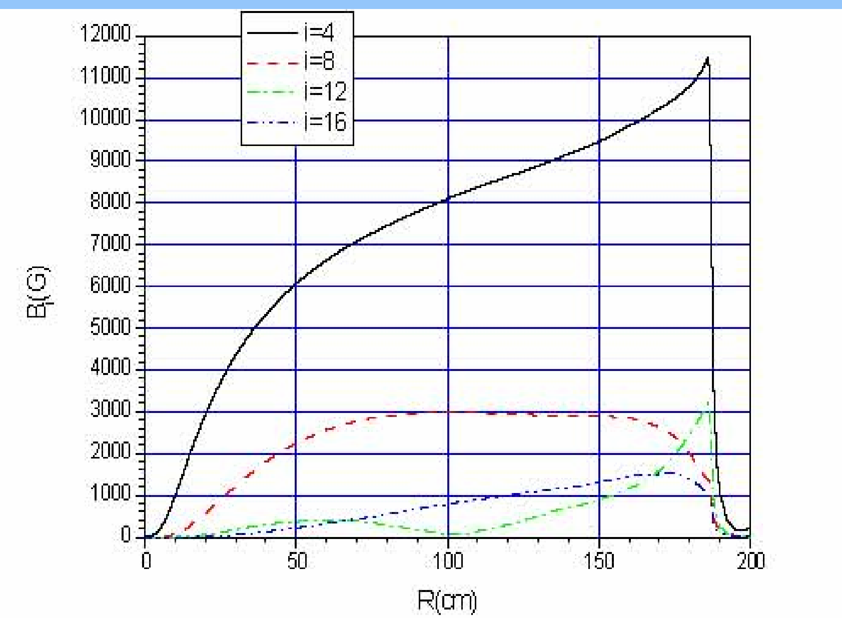
JINR magnetic field simulation of C400





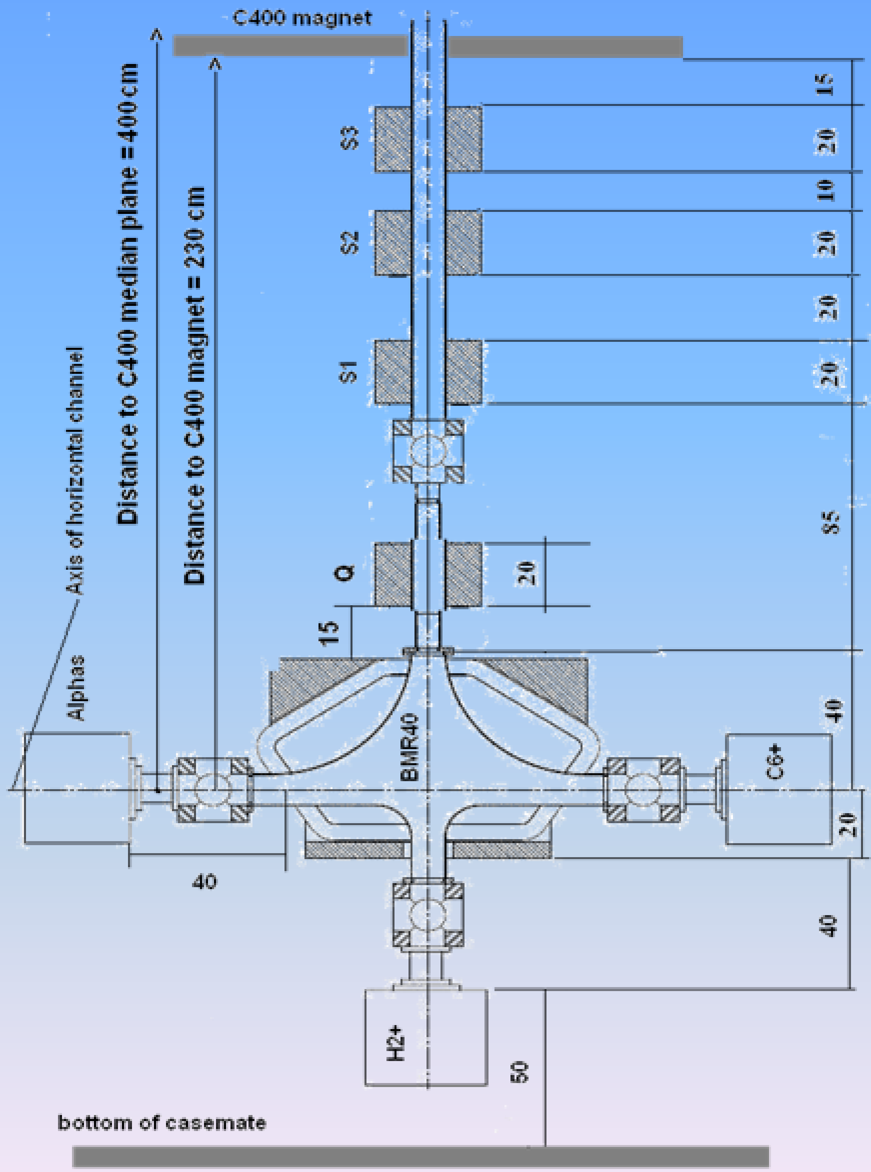


Average magnetic field



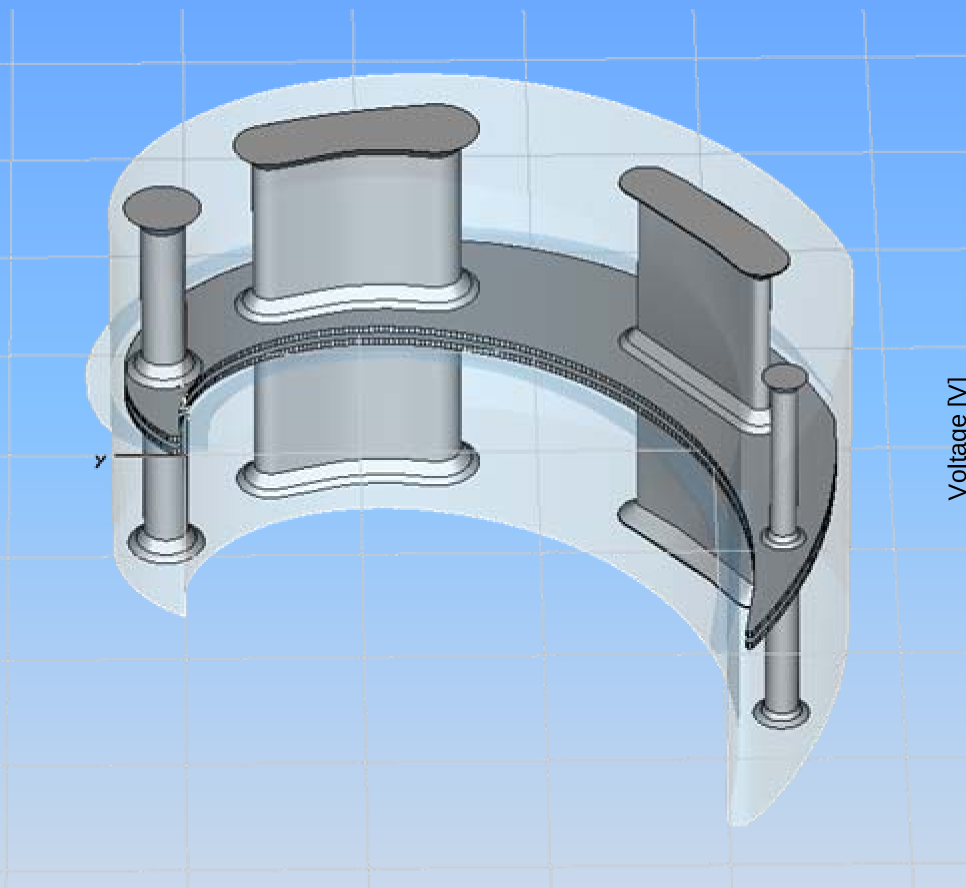
Main harmonics of the cyclotron magnetic field

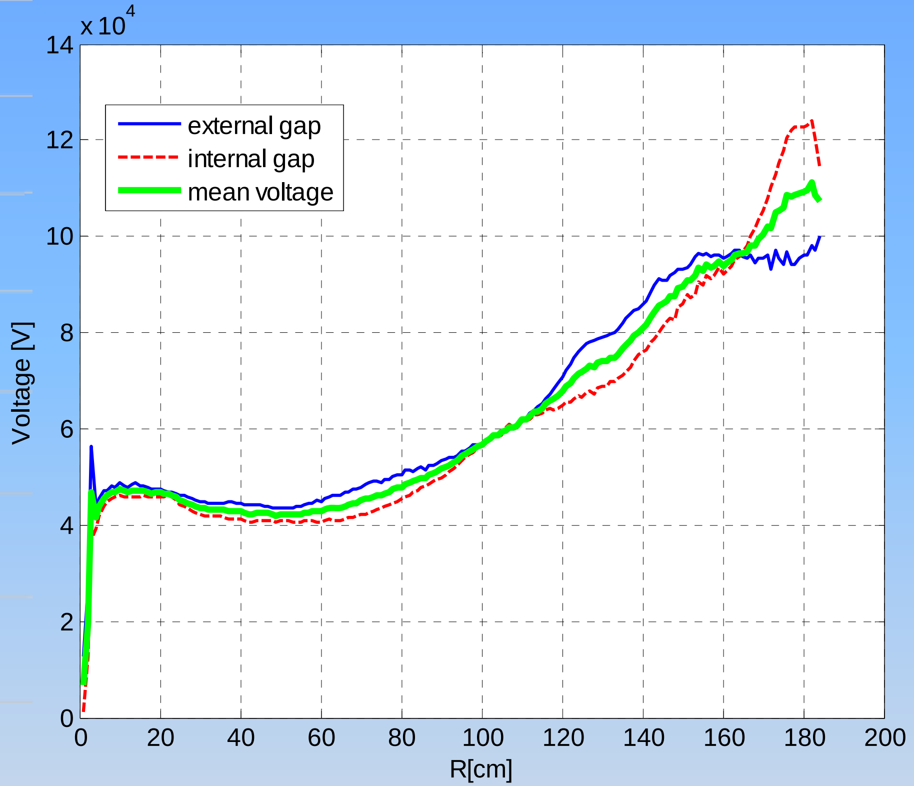
C 400 injection line



C^{6+} carbon ion source, I=3 μA

RF cavity simulations





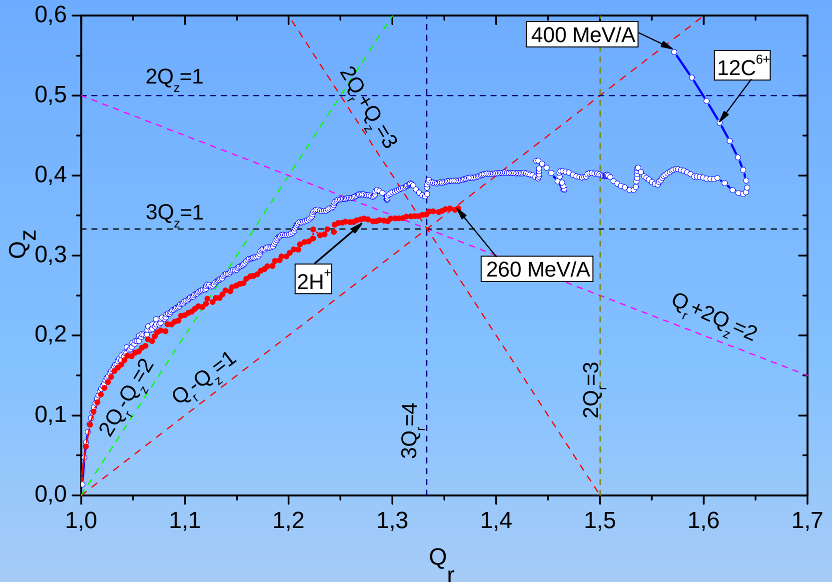
View of the cavity model. Voltage distribution along the gap

Each dee will be supported by 2 flat pillars and 2 circular pillars in a half-wave resonator.

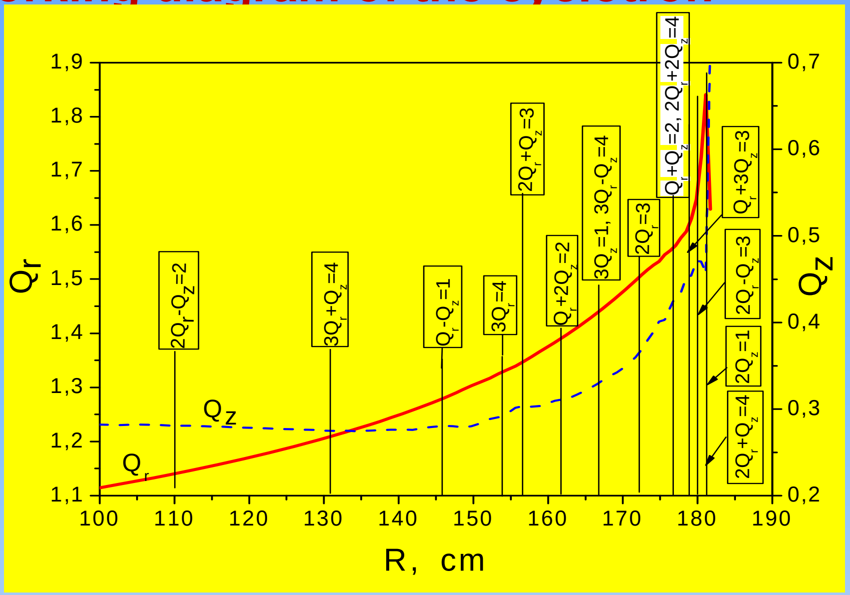
Each cavity is powered by a 76 MHz, 100 kW tetrode based amplifier

The cyclotron will have two 45° dees, operating on the 4th harmonic mode

Particle acceleration in C400



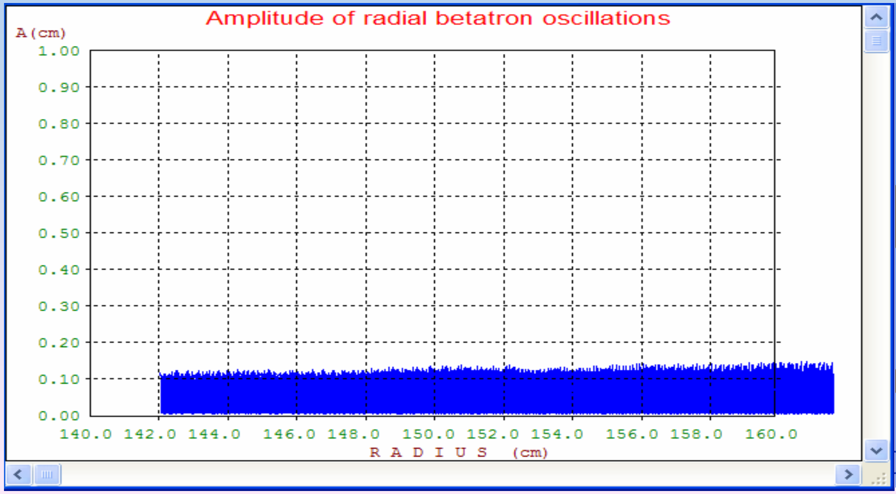
Working diagram of the cyclotron



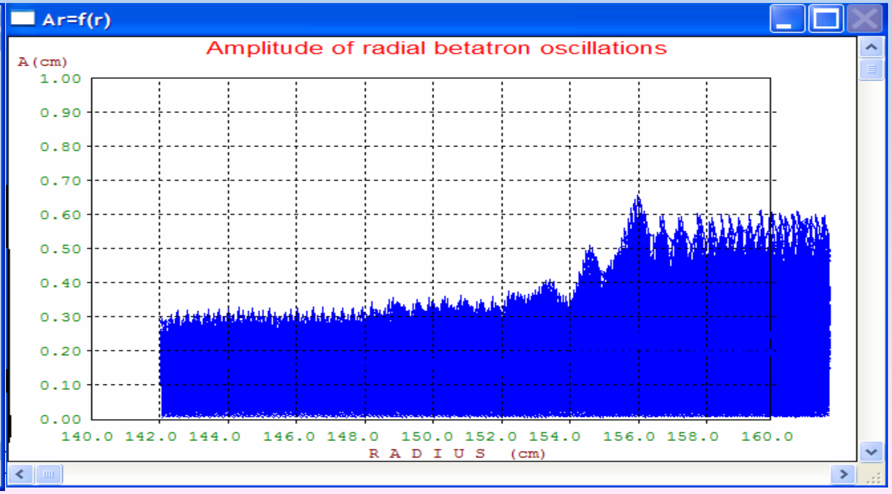
Passing through resonances at large radiuses

3 Qr = 4 resonance

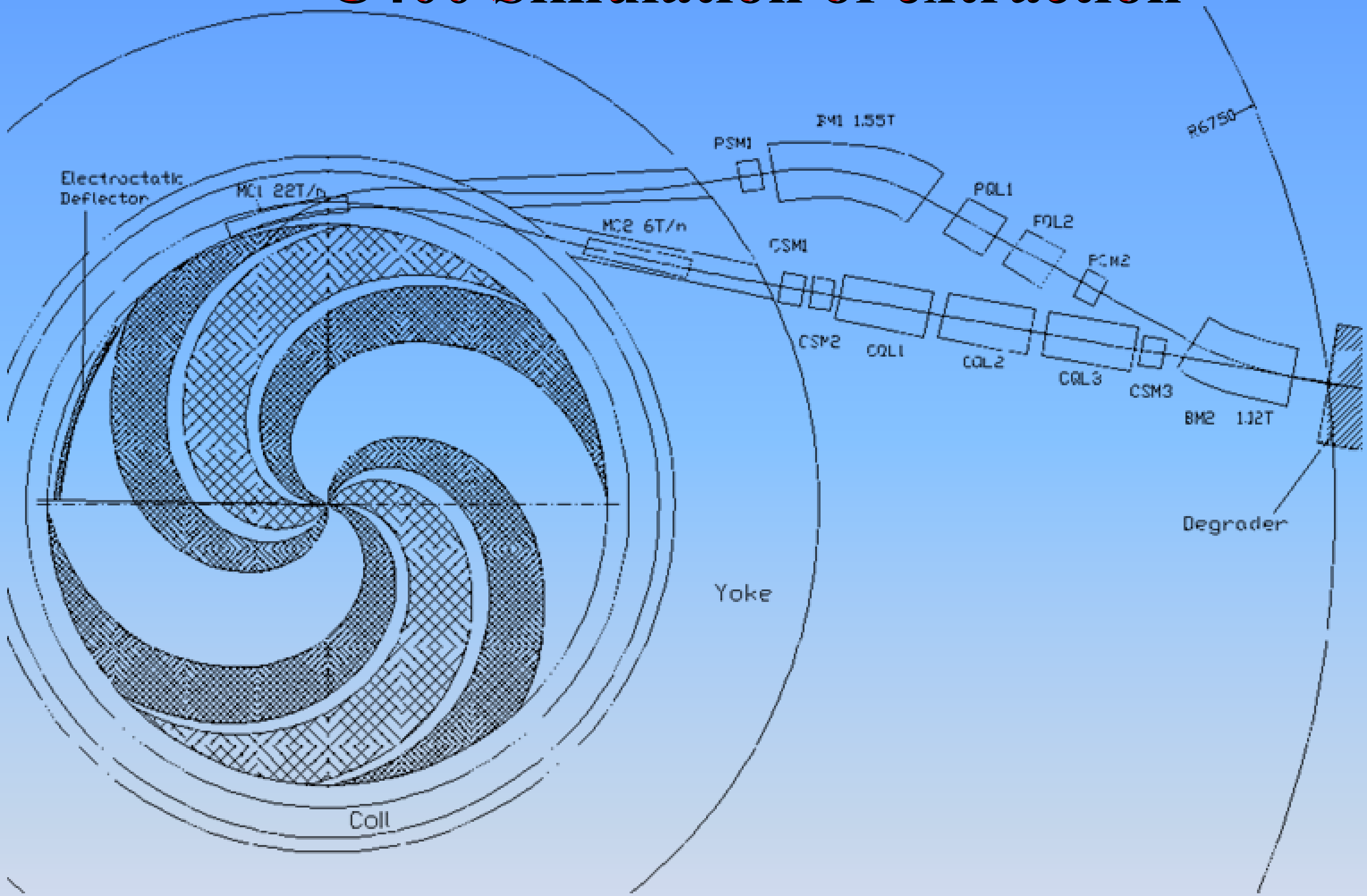
Ar initial =1 mm



Ar initial=3 mm



C400 Simulation of extraction



Extraction of protons by the stripping foil.

Minimal proton energy for 2-turn extraction is 265 MeV.

Extraction of carbon beam by electrostatic deflector with 140 kV/cm field inside.

The extraction efficiency was 73%.

Both beams have a spot size of $\sigma_{x,y}$<1 mm at degrader point.

The IBA compact carbon gantry

The gantry of Heidelberg (20 m long, 12 m diameter, 600 Tons)

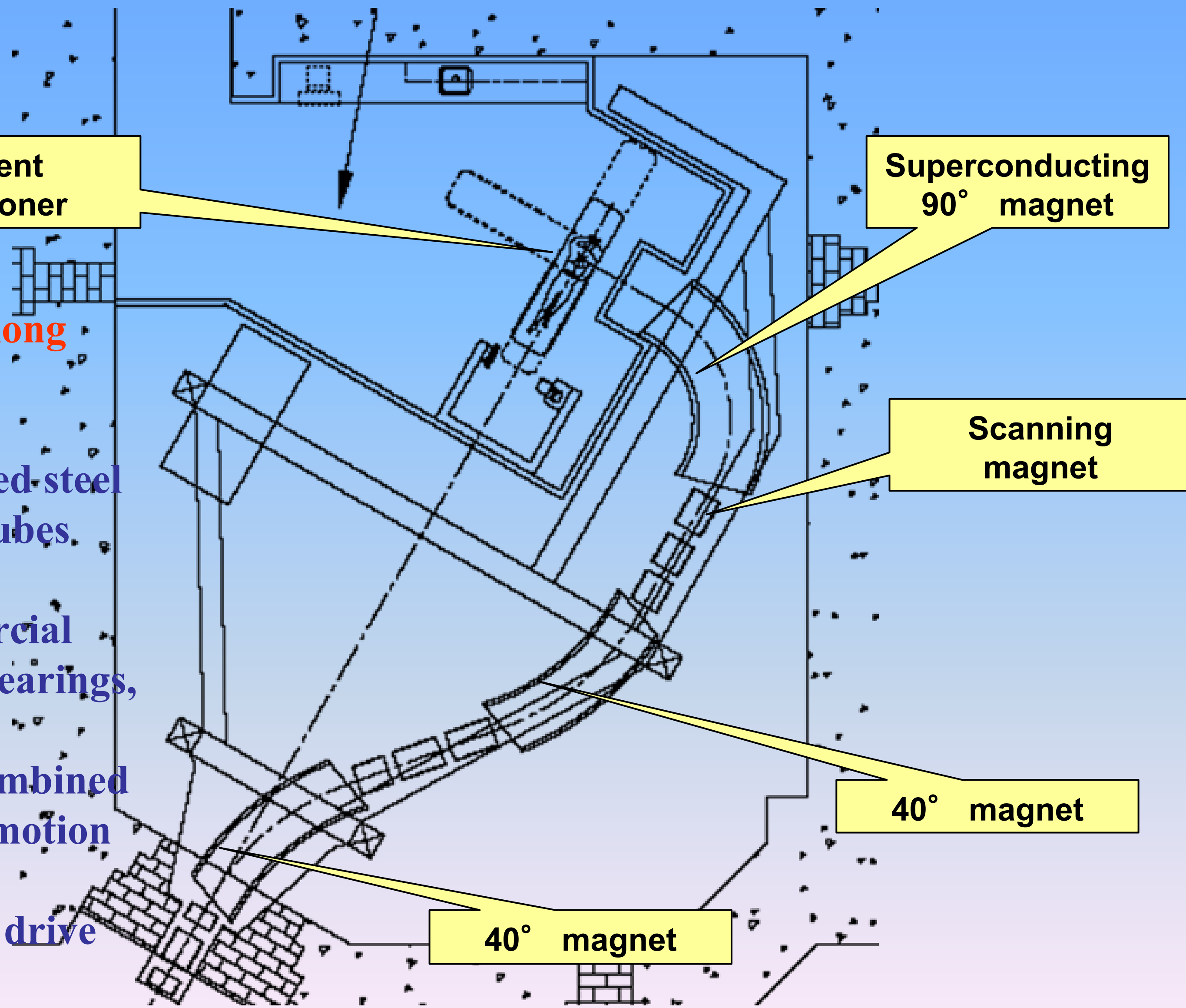
9.2 m diameter, 12.7 m long
156 Tons rotating mass

Structure made of welded steel plates and reinforcing tubes

Use of standard commercial self-aligning spherical bearings,

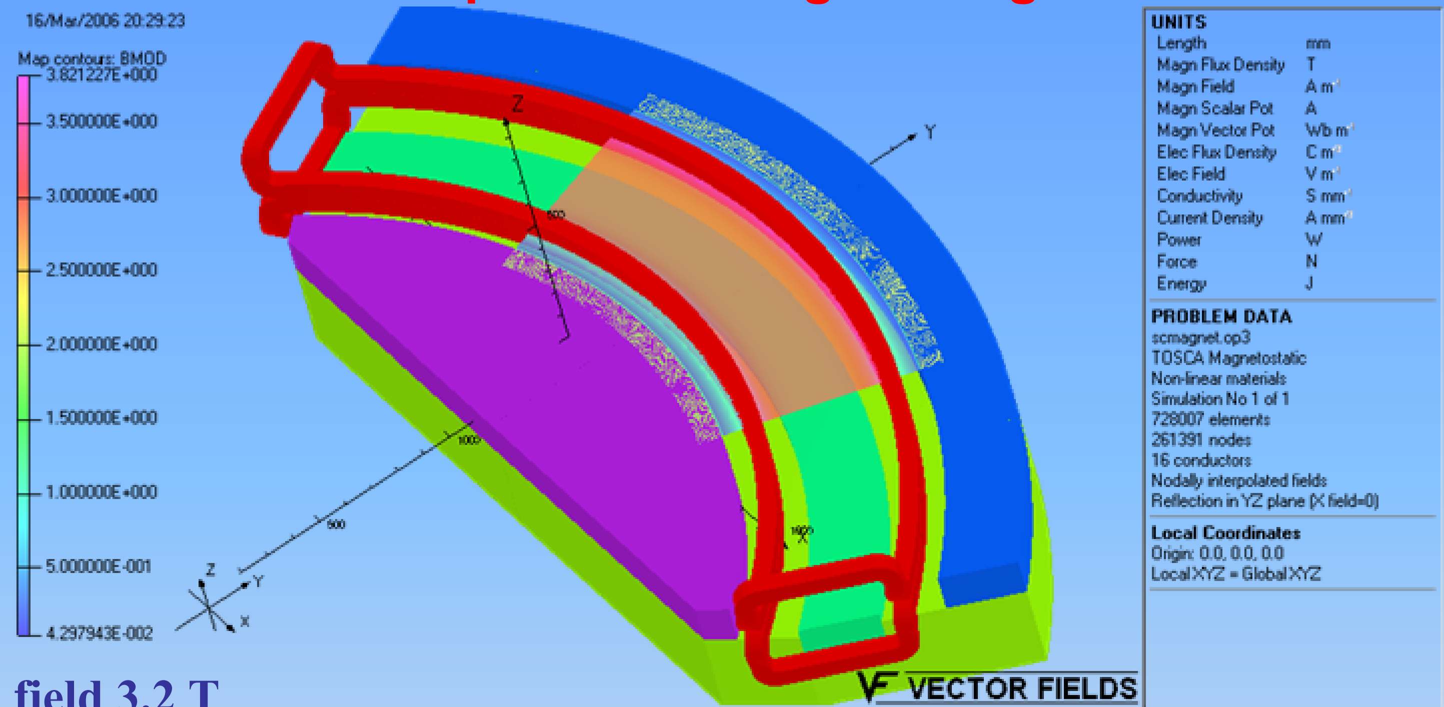
180° gantry rotation, combined with patient positioner motion

Drive by multiple chain drive on single motor



Field size 20 x 20 cm at isocenter

Tosca simulation of the superconducting 90°magnet

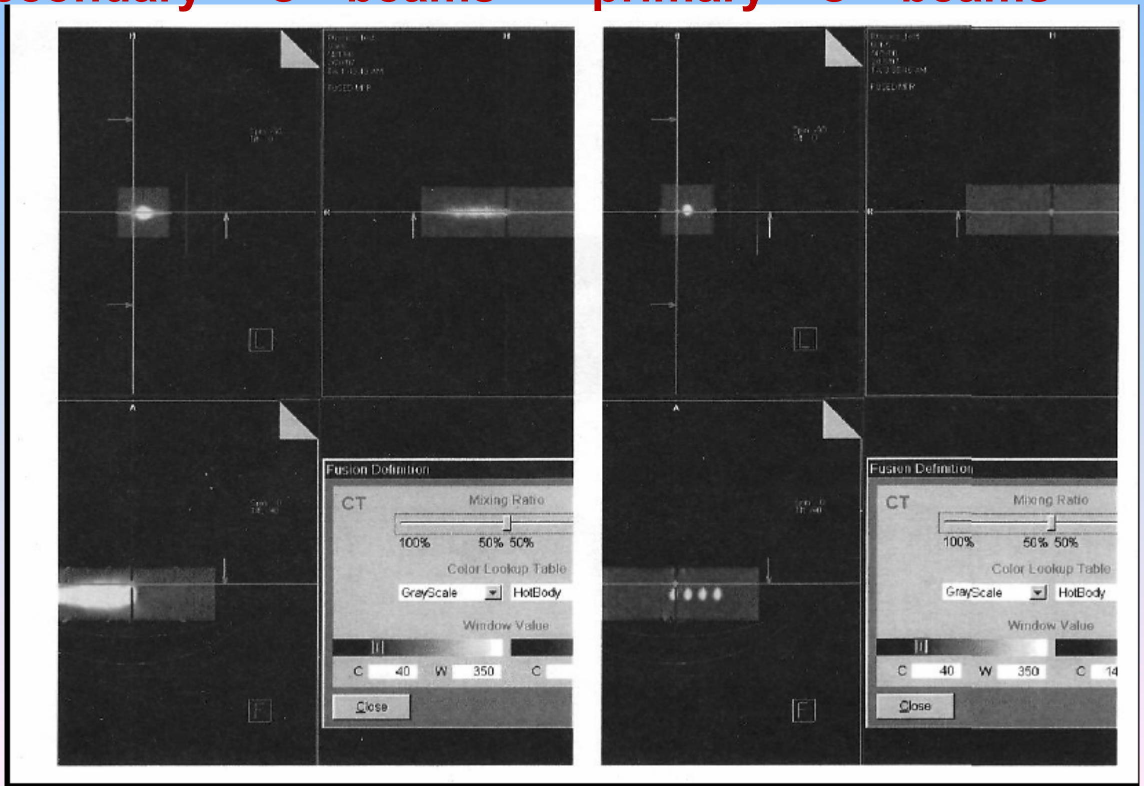


Bending radius 2 m, field 3.2 T
Space for beam: 20 x 20 cm for scanning with scanning magnets upstream
15° pole face angle
Ni-Ti superconducting wire, 80 A/mm²
Rotatable magnet => no helium bath
Coil cooled by four Sumitomo 4°K cryocoolers
Weight: 28 Tons
Stored energy: 8.5 MJ
Maximum rate of field change 1T/minute

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

- 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



FORMATION OF PRIMARY RADIOACTIVE CARBON ION BEAMS

Cancer therapy and on-line PET dose verification with use of ^{11}C beams (400 MeV/n):

^{11}C life-time ~20 minutes

^{11}C produced in reaction:

1) $p + {}^{14}N \rightarrow {}^{11}C + \ldots$;

2) chemical reaction $^{11}C + 2H^2 \rightarrow {}^{11}CH^4$;

3) separation CH^4 and N_2.

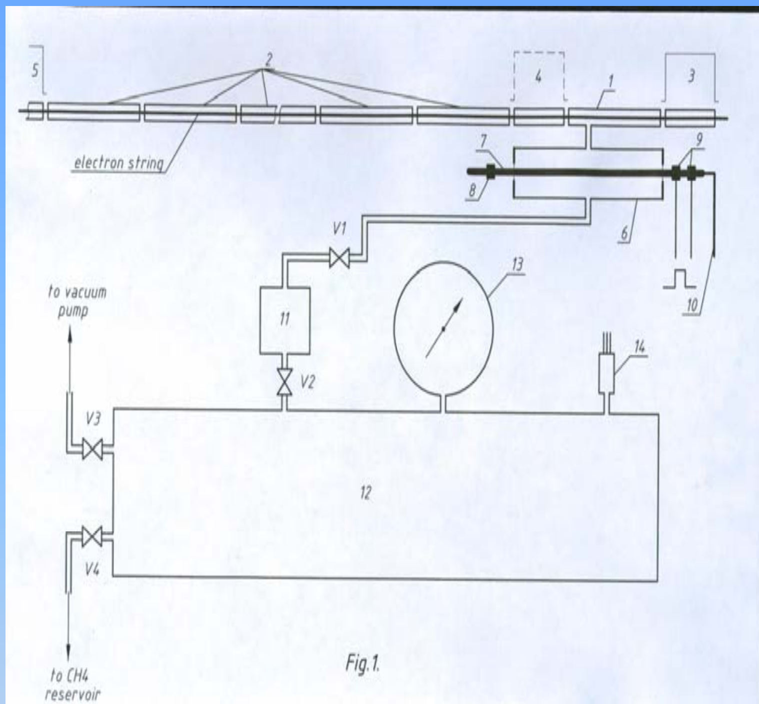
Production of the intense beams of $^{11}C^{6+}$ (10^{10}-10^{11} pps) is possible if the conversion efficiency of methane to $^{11}C^{6+}$ is high.

10^{14} methane atoms in each 20min cycle.

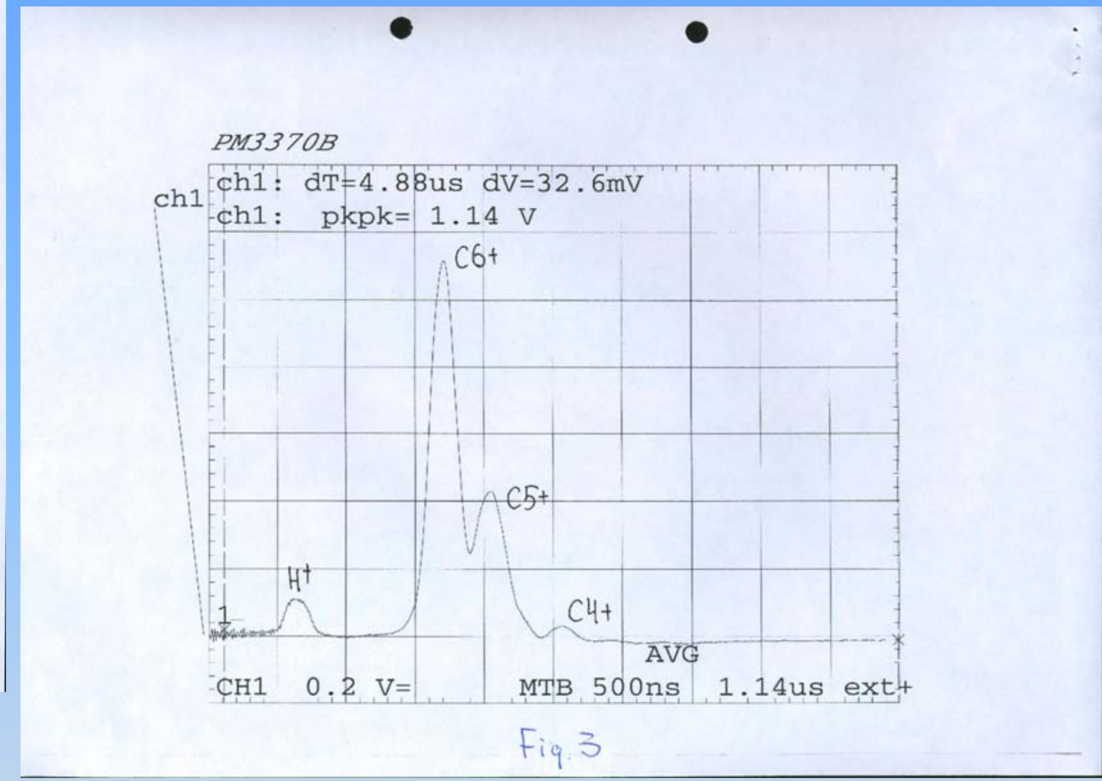
The main point: construction of "cell" for pulse injection of $^{11}CH^4$, which provides pulse injection of methane during injection time and absence of injection later untill the next pulse.

Electron String Ion Source,
used for production of radioactive ions $^{11}C^{6+}$ applied simultaneously for carbon treatment and PET (Collaboration with NIRS, Japan)
Dose verification at cancer treatment

Charge states spectra (10 ms inj.+ 50 ms ionization)



Experimental set-up for pulse injection of methane into Krion-2



The elaborated cryogenically based technology of accumulation and pulse injection of methane into electron string has been experimentally demonstrated.

The measured conversion efficiency appeared to be rather high in ESIS Krion-2:
methane (CH_4) -> C^{6+} 12-15 %.

This makes use of ESIS for this kind of a cancer therapy uniquely favourable ion source

Conclusion

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

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

The treatment capability of hospital center of hadron therapy is about 1000 patients/year.

About 30-40 Center of proton therapy and 10-15 Centers of carbon therapy should be constructed in Russia.