CENTERS OF HADRÓN THERAPY ON THE BASIS
OF CYCLOTRONS

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JINR MEDICAL TECHNICAL COMPLEX

REQUIREMENTS 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
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

\[
\Delta E = 2\xi \ln\left(\frac{E_{\text{max}}}{I} - \beta^2\right)
\]

\[
\xi = 0.15 \frac{MeV \ cm^2}{g} \frac{Z_i^2 Z_t}{\beta^2 A_t} \rho x
\]

\(\rho\) - density, \(x\) – target thickness, \(Z_i\) - 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
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 Research Center of Russian Medical Academy of Science.
Prostate treatment equipment

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

Cancer treatment in cabin №1
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%.
First scatter is a plate. Central part of Second scatter is constructed from a material at $Z \approx 100$ (Fig. c), boundary part from material at $Z \approx 6-10$ (Fig. d).

Homogeneity of dose transverse distribution of $\pm 2\%$ (Fig. b)

Efficiency of beam utilization of 30-40\%.
## Parameters of proton medical beams

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal energy, MeV</td>
<td>230-250</td>
</tr>
<tr>
<td>Depth of penetration, mm</td>
<td>30</td>
</tr>
<tr>
<td>Beam intensity at cancer treatment, p/s</td>
<td>$5 \times 10^9$</td>
</tr>
<tr>
<td>Maximal dose rate, Gy/l/min</td>
<td>2</td>
</tr>
<tr>
<td>Irradiation dose Gy/fraction</td>
<td>2</td>
</tr>
<tr>
<td>Number of fractions</td>
<td>20-30</td>
</tr>
<tr>
<td>Treatment time, min</td>
<td>2</td>
</tr>
<tr>
<td>Homogeneity of irradiation dose, %</td>
<td>±2.5</td>
</tr>
<tr>
<td>Maximal tumor volume at passive scanning, l</td>
<td>7.5</td>
</tr>
<tr>
<td>Maximal tumor volume at active scanning, l</td>
<td>2</td>
</tr>
<tr>
<td>Maximal scanning size on target, cm</td>
<td>20·20</td>
</tr>
<tr>
<td>Spot size of pencil beam, mm</td>
<td>3</td>
</tr>
<tr>
<td>Parameter</td>
<td>Cyclotron</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Energy of extracted particles</td>
<td>fixed</td>
</tr>
<tr>
<td>Energy variation rate, MeV/s</td>
<td>15</td>
</tr>
<tr>
<td>Energy spread, %</td>
<td>0.5</td>
</tr>
<tr>
<td>Stability of energy, %</td>
<td>0.1</td>
</tr>
<tr>
<td>Maximal beam current, nA</td>
<td>300</td>
</tr>
<tr>
<td>Current modulation time, ms</td>
<td>1</td>
</tr>
<tr>
<td>Extraction efficiency, %</td>
<td>60-80</td>
</tr>
<tr>
<td>Beam utilization, %</td>
<td>50</td>
</tr>
<tr>
<td>Working cycle, %</td>
<td>100</td>
</tr>
<tr>
<td>Emittance of extracted beam, π·mm·mrad</td>
<td>5</td>
</tr>
<tr>
<td>Diameter of accelerator, m</td>
<td>4-5</td>
</tr>
<tr>
<td>Weight, t</td>
<td>200-250</td>
</tr>
</tbody>
</table>
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).
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

Advantages:

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

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 $\pm10\%$ in this case.
## Parameters of proton isochronous cyclotron C235

<table>
<thead>
<tr>
<th>General parameters</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton energy, MeV</td>
<td>235</td>
</tr>
<tr>
<td>Internal current, nA</td>
<td>300</td>
</tr>
<tr>
<td>Beam emittances, $\pi \cdot \text{mm} \cdot \text{mrad}$</td>
<td>12/11</td>
</tr>
<tr>
<td>Magnetic field (min/max) T</td>
<td>0.9/2.9</td>
</tr>
<tr>
<td>Number of sectors</td>
<td>4</td>
</tr>
<tr>
<td>Magnet diameter, m</td>
<td>4.3</td>
</tr>
<tr>
<td>Radius of beam extraction, m</td>
<td>1.08</td>
</tr>
<tr>
<td>Elliptical hill gap, cm</td>
<td>9.6/0.9</td>
</tr>
<tr>
<td>Duant aperture, cm</td>
<td>2</td>
</tr>
<tr>
<td>RF frequency, MHz</td>
<td>106.1 (4 harmonic)</td>
</tr>
<tr>
<td>Dee voltage, (min/max) kV</td>
<td>60/130</td>
</tr>
<tr>
<td>Ion source</td>
<td>PIG, internal</td>
</tr>
<tr>
<td>Electrostatic deflector field, kV/cm</td>
<td>170</td>
</tr>
<tr>
<td>Extraction efficiency, %</td>
<td>60</td>
</tr>
<tr>
<td>Power, kW</td>
<td>446</td>
</tr>
<tr>
<td>Weight, t</td>
<td>220</td>
</tr>
</tbody>
</table>
Active Spot Pencil Beam Scanning technique was developed in PSI cyclotron center of proton therapy. $\sigma=3\text{mm}$, 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 gantry 2
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, $\sigma=3$ mm
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
1 min-1Gy-1 liter
Dead time-1.5 min=
sweeper (10 000\cdot3 ms)+table(21\cdot1 s)+shifter(21\cdot21\cdot50 \, ms)
Duty factor -50%
Planed PSI IMPT  
at active PBS with gantry 2

Intensity modulated line and contour scanning

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

Zoom of beam size at 177 MeV vs. Gantry Angle

Cyclotron tuning
Non Gaussian distribution in horizontal phase space of extracted synchrotron proton beam

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 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
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

Simulation extraction efficiency is approximately 71.4% - at amplitude of radial oscillation of 4 mm.

r.m.s-sizes of extracted proton beam
JINR-IBA C400 Design applied for carbon therapy
# Parameters of the C400 cyclotron

<table>
<thead>
<tr>
<th><strong>General properties</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>accelerated particles</td>
<td>( \text{H}_2^+, \text{He}^2+, (\text{Li}^3+), (\text{B}^5+), \text{C}^6+ )</td>
</tr>
<tr>
<td>Injection energy</td>
<td>25 keV/Z</td>
</tr>
<tr>
<td>final energy of ions, protons</td>
<td>400 MeV/amu</td>
</tr>
<tr>
<td>extraction efficiency</td>
<td>70 % (by deflector)</td>
</tr>
<tr>
<td>number of turns</td>
<td>( \sim ) 1700</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th><strong>Magnetic system</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>total weight</td>
<td>700 tons</td>
</tr>
<tr>
<td>outer diameter</td>
<td>6.6 m</td>
</tr>
<tr>
<td>height</td>
<td>3.4 m</td>
</tr>
<tr>
<td>Pole radius</td>
<td>1.87 m</td>
</tr>
<tr>
<td>valley depth</td>
<td>60 cm</td>
</tr>
<tr>
<td>bending limit</td>
<td>( K = 1600 )</td>
</tr>
<tr>
<td>hill field</td>
<td>4.5 T</td>
</tr>
<tr>
<td>valley field</td>
<td>2.45 T</td>
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</table>

<table>
<thead>
<tr>
<th><strong>RF system</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>radial dimension</td>
<td>187 cm</td>
</tr>
<tr>
<td>vertical dimension</td>
<td>116 cm</td>
</tr>
<tr>
<td>Frequency</td>
<td>75 MHz</td>
</tr>
<tr>
<td>Operation</td>
<td>4\textsuperscript{th} harmonic</td>
</tr>
<tr>
<td>number of dees</td>
<td>2</td>
</tr>
<tr>
<td>dee voltage: center/extraction</td>
<td>80/170 kV</td>
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</table>
## Cyclotron efficiencies and currents

<table>
<thead>
<tr>
<th></th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>3000 enA</td>
</tr>
<tr>
<td>Axial injection</td>
<td>90.00%</td>
</tr>
<tr>
<td>Central region</td>
<td>25.00%</td>
</tr>
<tr>
<td>Acceleration</td>
<td>90.00%</td>
</tr>
<tr>
<td>Extraction</td>
<td>65.00%</td>
</tr>
<tr>
<td>Total efficiency</td>
<td>13.16%</td>
</tr>
<tr>
<td>Extracted current</td>
<td>394.9 enA</td>
</tr>
</tbody>
</table>
JINR magnetic field simulation of C400

Average magnetic field

Main harmonics of the cyclotron magnetic field

Z(cm)

R(cm)

0 50 100 150 200 250 300

0 50 100 150 200 250 300

R(cm)

Z(cm)

R(cm)

R187
R207
R221.8
R232
R238
R303

yoke
sector
C 400 injection line

C\textsuperscript{6+} carbon ion source, I=3 \( \mu \text{A} \)
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

Passing through resonances at large radiuses

Ar initial = 1 mm

Ar initial = 3 mm
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
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 $^{11}\text{C}^6^+$

- On-line dose verification at carbon treatment by high intensive radioactive $^{11}\text{C}^6^+$ ion beams
- High radioactive ion intensity $^{11}\text{C}^6^+$ required for cancer treatment and simultaneously on-line PET tomography
- High resolution at direct application of primary radioactive $^{11}\text{C}^6^+$ ion beam comparing with radioactive secondary beams produced in tumor target.
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 +...;
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.
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 (CH₄) → C₆⁺ 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.