ADVANCED ACCELERATOR SYSTEMS FOR CANCER THERAPY

Accelerator-based neutron source for boron neutron capture therapy (BINP,NSU, BTG);
Proton/Ion Synchrotrons (BINP);
Proton Synchrotron (PROTOM.RU, Protvino)

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Cancer diagnostics and visualization

Наноматериалы и наноустройства на основе нуклеиновых кислот

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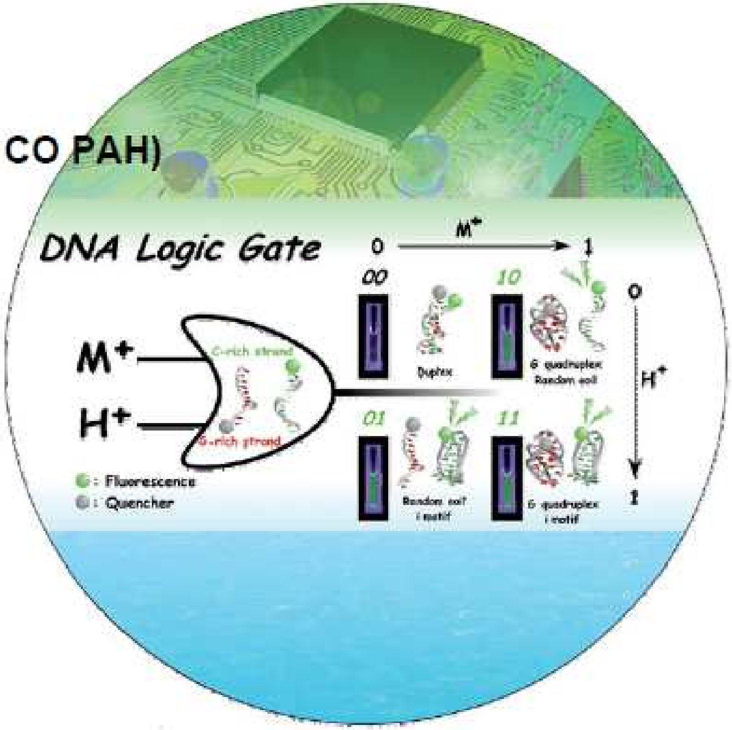
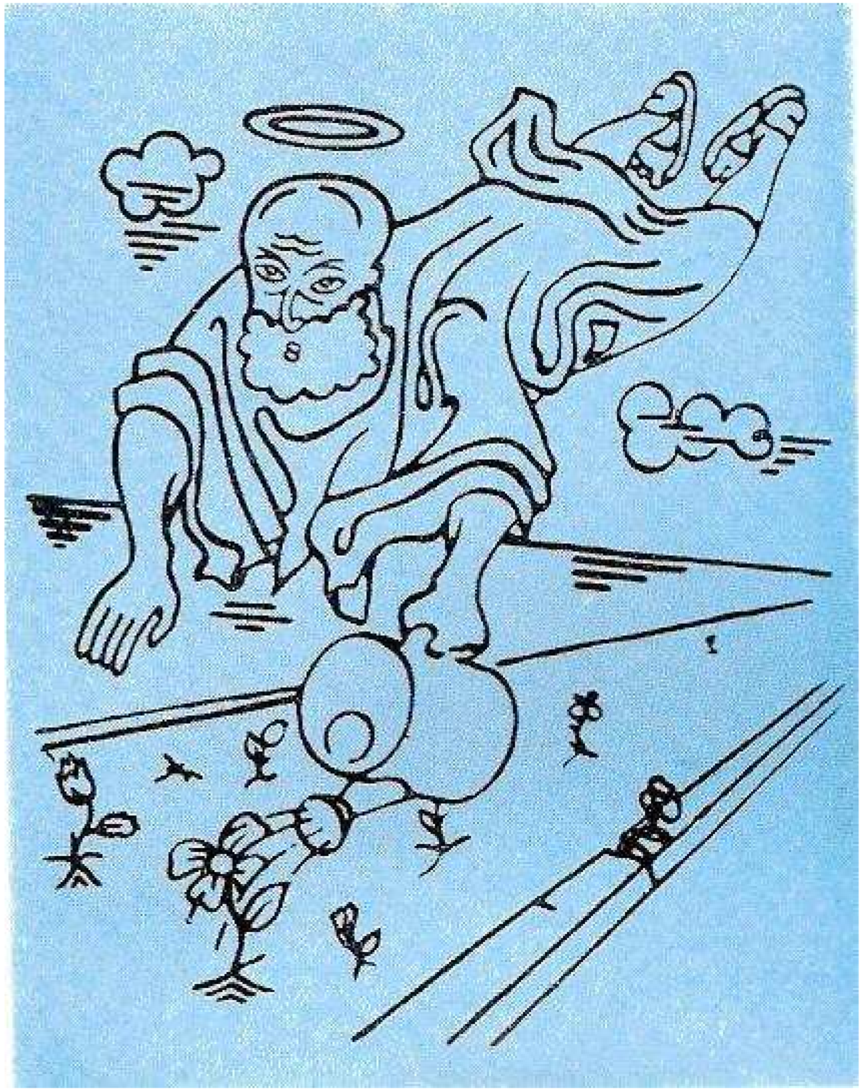


some Textes are translated today

Invited talk by vlassov
2006 academy session

G.I. Budker, founder and director of INP

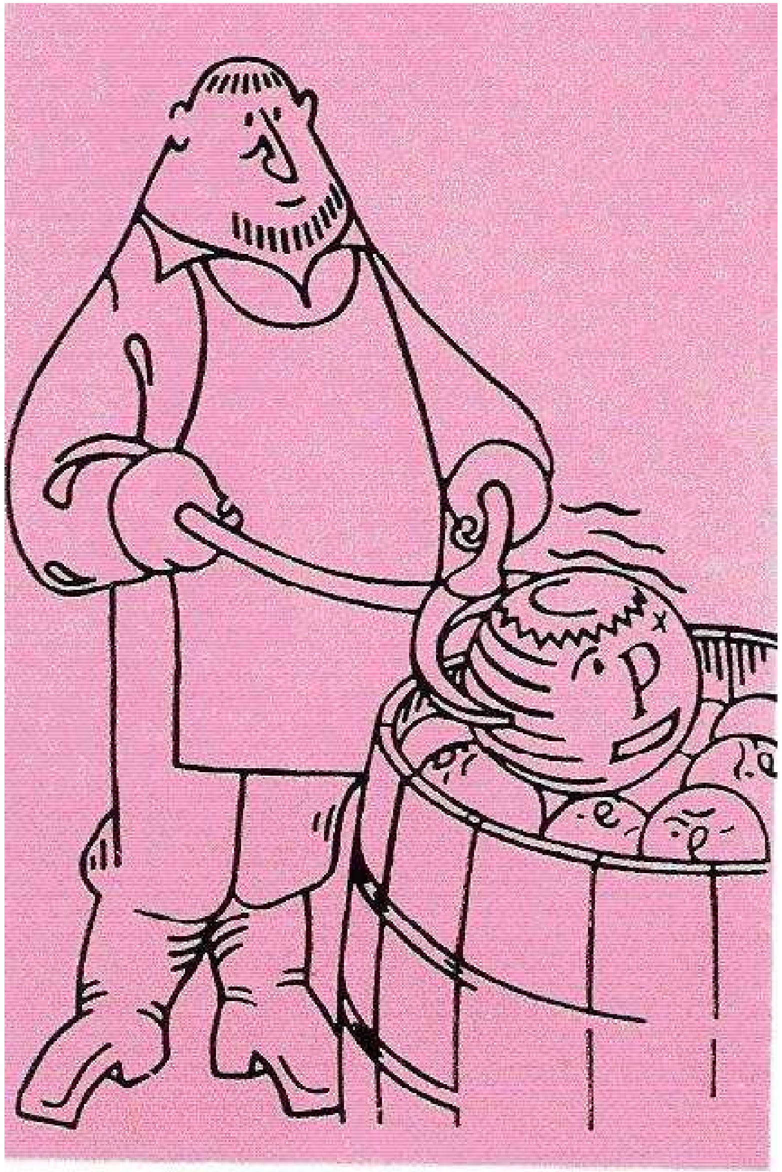


Round table BINP

King Arthur Pub

Round table of BINP is the method of problems solving

Traditional Siberian folk's handicrafts in BINP:



Electron cooling;

Siberian Snakes;

Negative ion sources;

Neutral Beam Injectors;

Superconducting wigglers;

Sources of Polarized particles:

Industrial accelerators;

Storage Rings; Detectors…Physicists

Advanced Accelerator Systems for Cancer Therapy…

BNCT, Proton Synchrotrons, Ion Synchrotrons…..

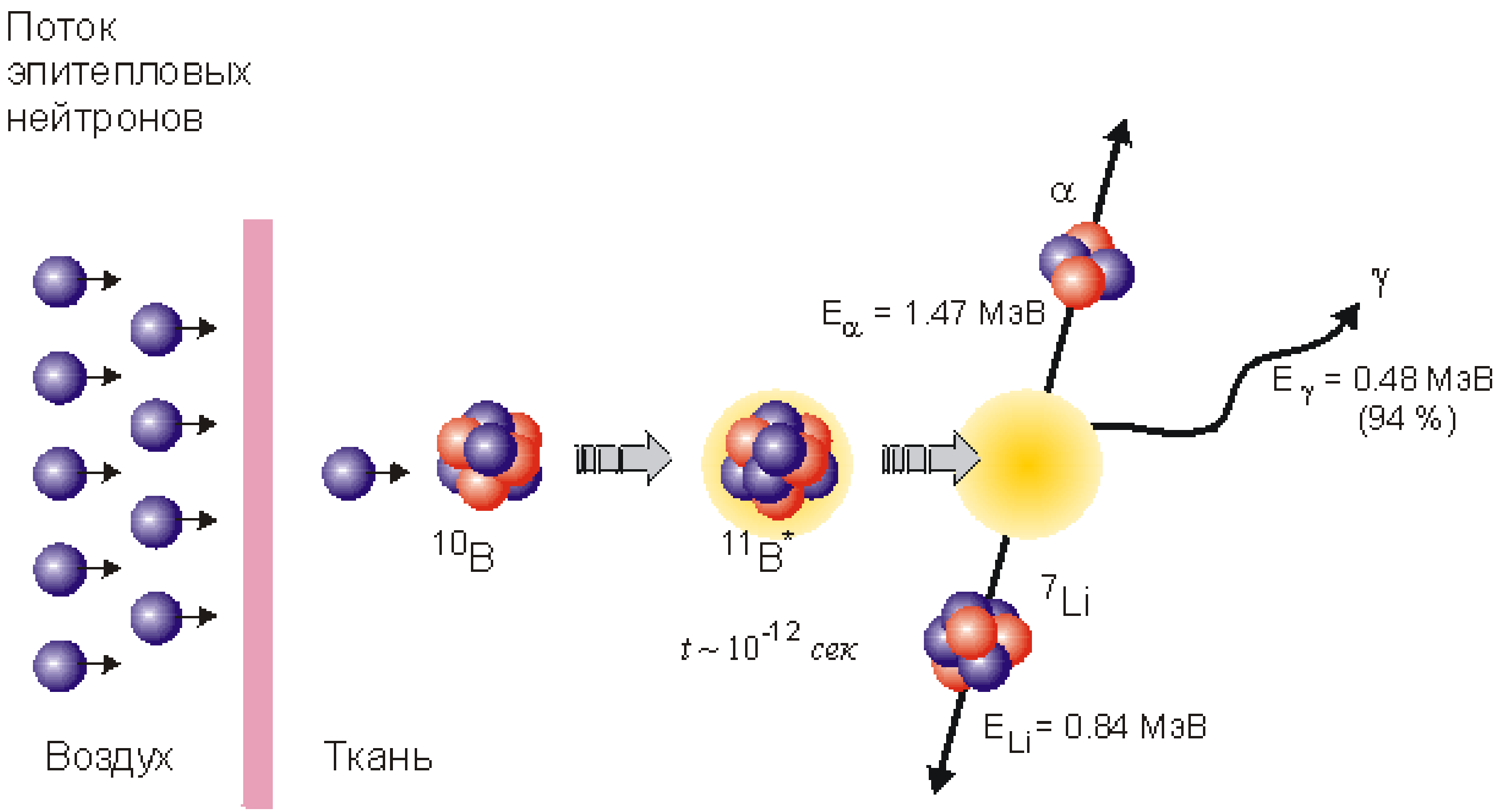
Export orientation

Layout of the talk

- What is BNCT?
- Accelerator-based neutron source for boron neutron capture therapy (BINP,NSU, BTG);
- Proton Synchrotron (PROTOM.RU, Protvino)
- Proton/Ion Synchrotrons (BINP);

BNCT fundamentals

$^{10}B(n,\alpha\ )^{7}Li$ (cross section 4010 barn)



Proposed - G.L.Locher (Franklin Institute at Pennsylvania) in 1936

Progress in compounds development:

*^{10}**B** concentration in tumor cells upto* 40 µg/g

^{10}B Enriched Compounds for Boron Neutron Capture Therapy:

$^{10}BC_9H_{12}NO_4$ d,l-p-Boronophenylalanine (D,L-BPA)

$^{10}BC_9H_{13}NO_4C$ d,l-p-Boronophenylalanine HCl (D,L-BPA.HCl)

$^{10}BC_9H_{12}NO_4$ l-p-Boronophenylalanine (L-BPA)

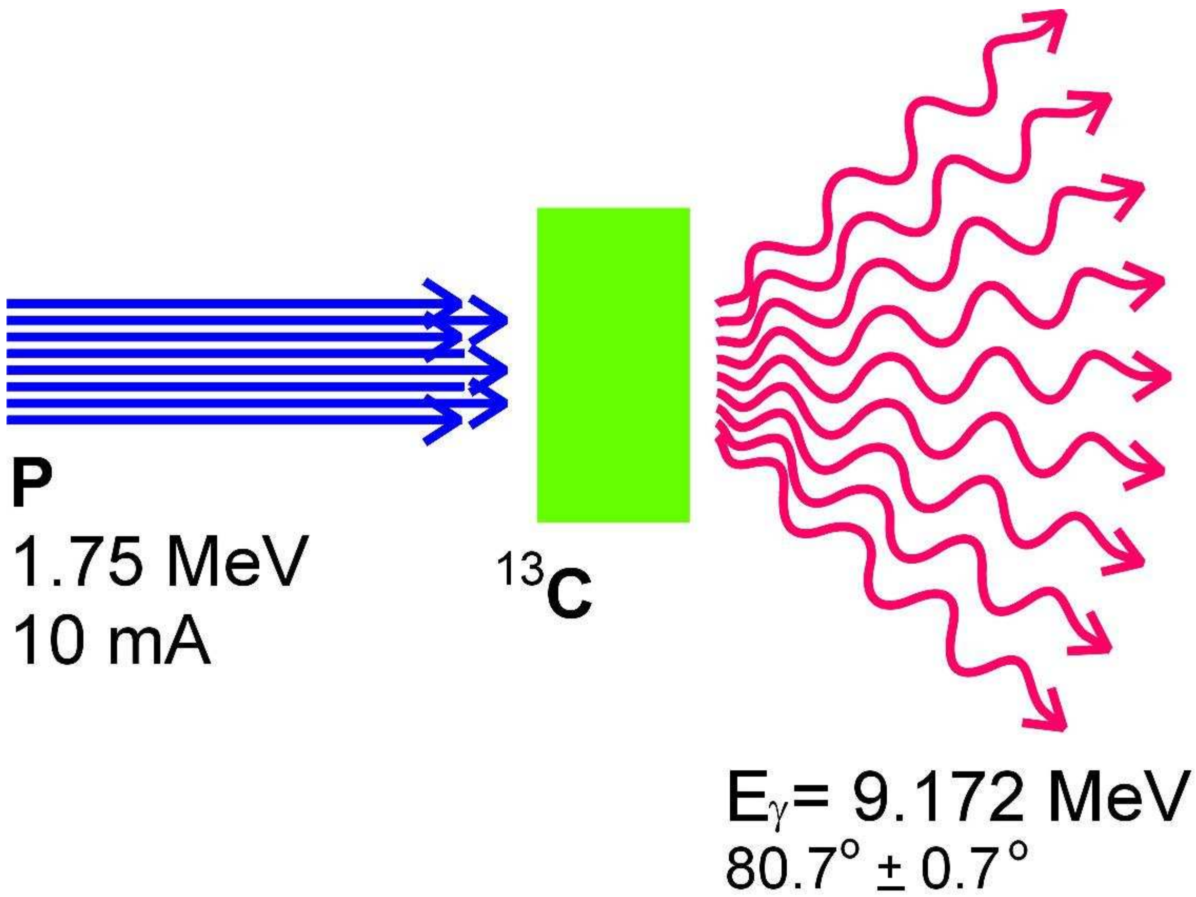
$^{10}BC_9H_{13}NO_4Cl$ l-p-Boronophenylalanine HCl (L-BPA.HCl)

$Cs_2{}^{10}B_{12}H_{11}SH$ Cesium Borocaptate (CsBSH)

$Na_2{}^{10}B_{12}H_{11}SH$ Sodium Borocaptate (NaBSH)

Gliobastoma of brain; spread cancer; Targeted Delivery Systems; Diagnostics; Visualizaton.

Resonance Gamma Ray Explosives detection (contain nitrogen)



ISTC Project # 2569:
"ACCELERATOR-BASED NEUTRON SOURCE FOR BORON NEUTRON-CAPTURE THERAPY"

Supported: 31 march, 2003
Duration: 24 months

Participating Institutions:

- Budker Institute of Nuclear Physics, Novosibirsk
- Russian Federal Nuclear Center — Institute of Technical Physics, Snezhinsk
- Institute of Physics and Power Engineering, Obninsk
- Medical Radiological Research Center of RAMS, Obninsk

Foreign Collaborators:

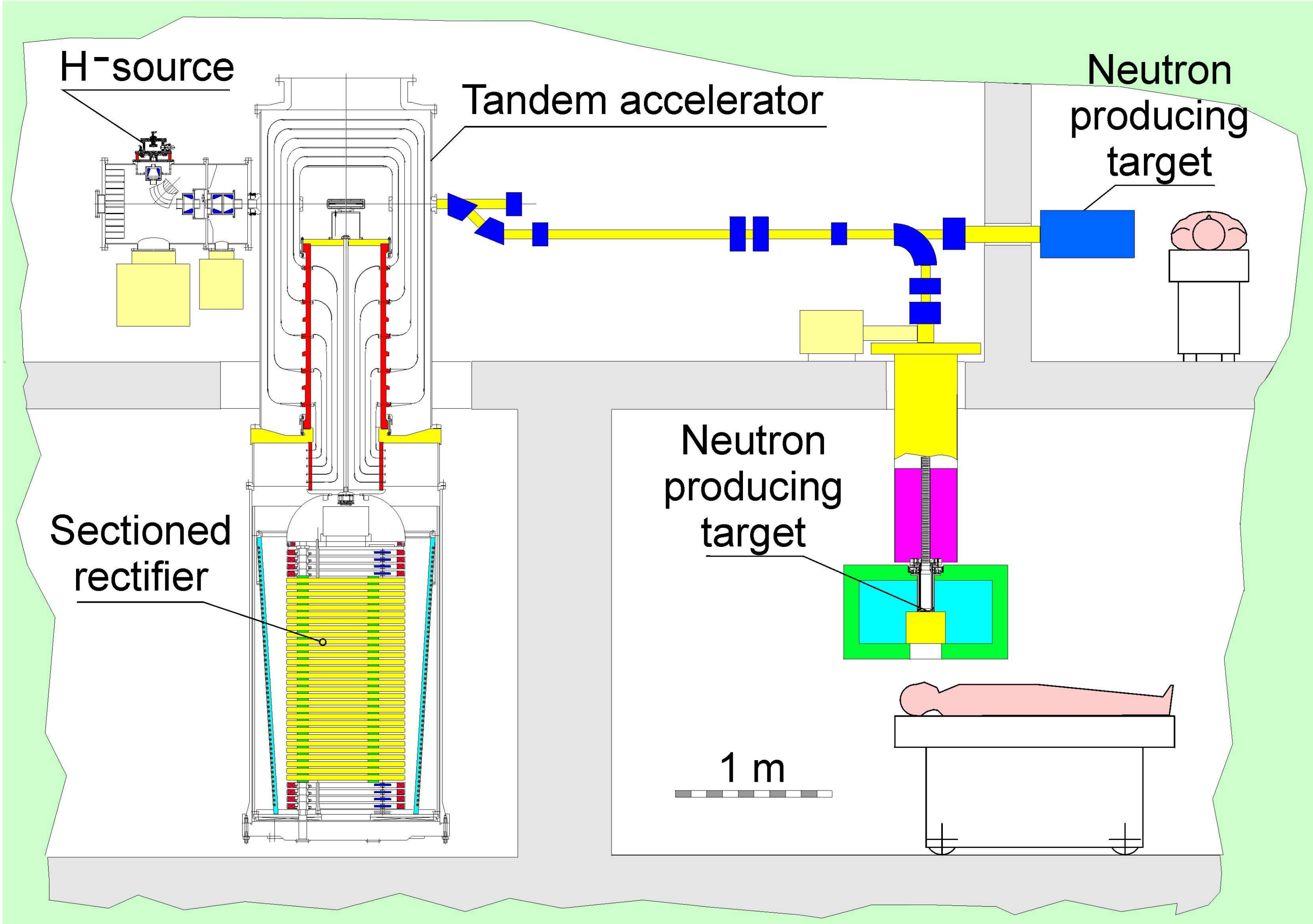
- Institut für Hochleistungsimpuls- und Mikrowellentechnik, Forschungszentrum Karlsruhe, Germany
- Research Reactor Institute, Kyoto University (KURRI), Osaka, Japan
- Technical Institute Kawasaki Heavy Industries, Ltd., Chiba, Japan
- Brookhaven Technology Group, Inc., USA
- Advanced Technology Development, Inc., USA

Objective: proof-of-principle experiment

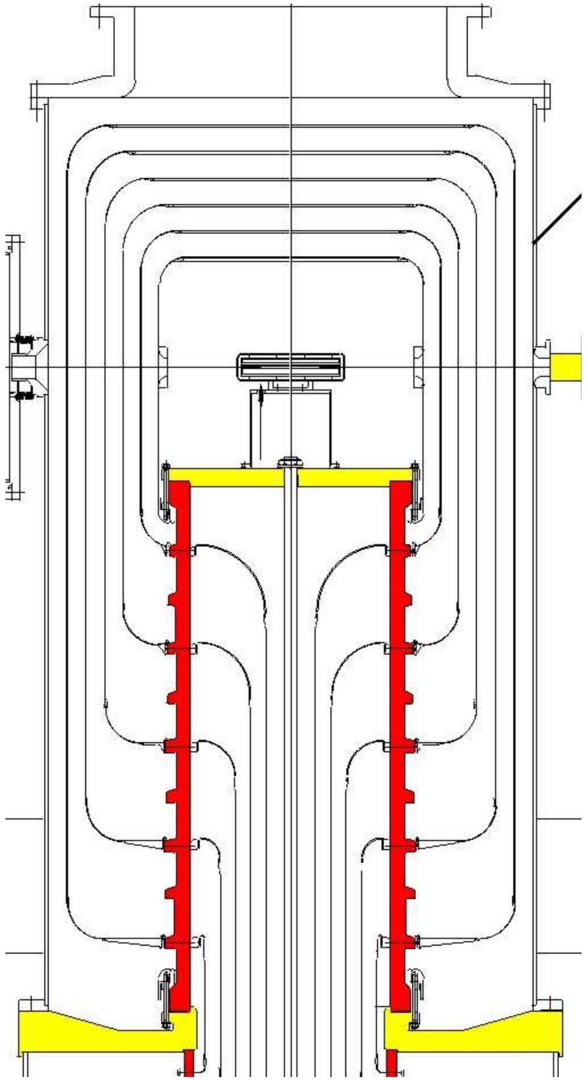
VITA BNCT TEAM (G. I. Silvestrov)

~30 Student's work from NSU NSTU

Accelerator-based neutron source for BNCT



Electrodes of the Vacuum Insulating Tandem Accelerator (VITA)



Neutron production

1. Generation of collimated neutron flux near $^{7}Li(p,n)^{7}Be$ reaction threshold with 1.915 MeV proton beam on target. Required thickness Of lithium target is several μm.

2. Neutron production with a higher energy proton beam (2.5MeV) on thick 100 μm target

Some problems

- **Heat removal from target at power density ~1 kW/ cm^2**
- **Stability of Li layer 2 – 3 μm thick.**
- **Lithium migration**
- **Damage of the target**
- **Removal of accumulating ^{7}Be-isotope**

Requirements to an accelerator

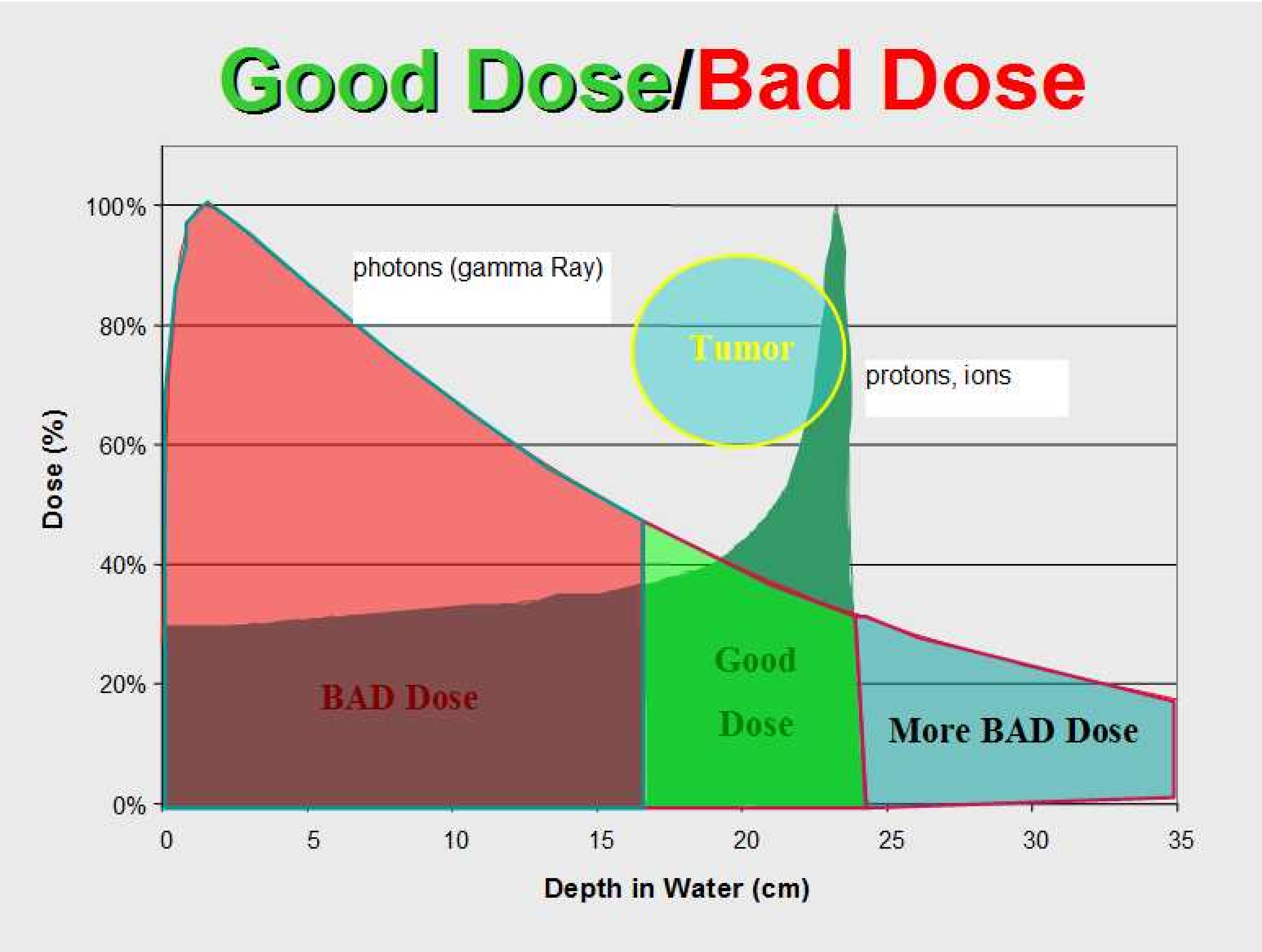
- Sufficient average current ($\geq$ 10 mA)
- Energy stability
- Simple enough service
- Low cost
- High availability

VITA, BNCT. 2 MeV; 3 mA

Contents

- Dose Distribution. Bragg Pick.
- High Dose in the end of Track.
- Current Status
- Present Systems
- PROTOM Synchrotron
- BINP Synchrotron

Dose distribution for Photons and Protons



Current Status - # of treated patients

- All accelerator based facilities (in operation and out of operation) since 50s:

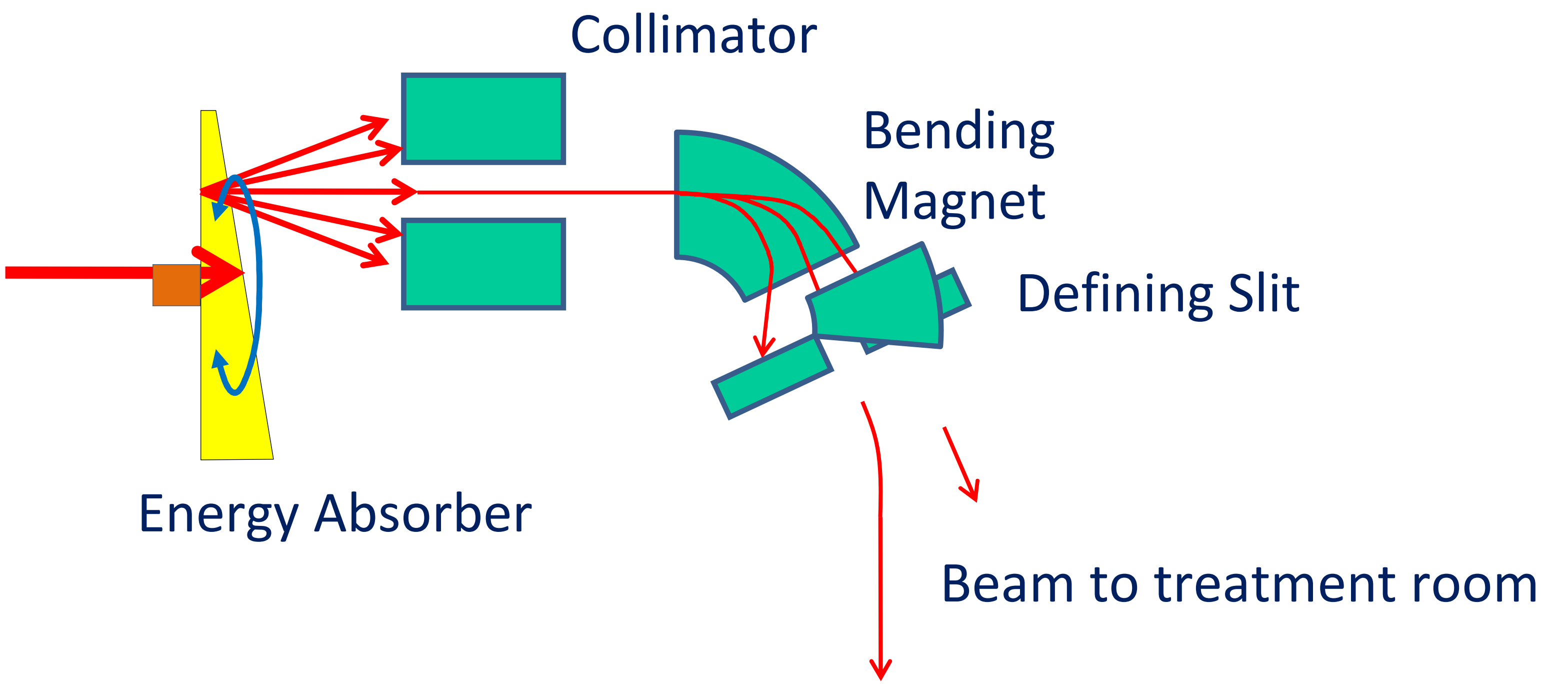
He	2,054
Pions	1,100
Other ions	873
C-ions	7,151
Protons	67,097
Grand Total	***78,275***

Current Status – treatment cost

Country	GDP US$	Treatment Cost per patient US$
USA	47,000	55,000
Japan	38,643	30,000 *NCCH etc.*
Germany	44,615	30,000 *GSI*
Taiwan	17,034	10,000 *CGMH*
China	3,232	30,000 *WJH*

Present Systems (Cyclotron)

- Cyclotron produces fixed energy protons - needs energy selection system:



Present Systems (Cyclotron)

- Beam delivery – passive scanning

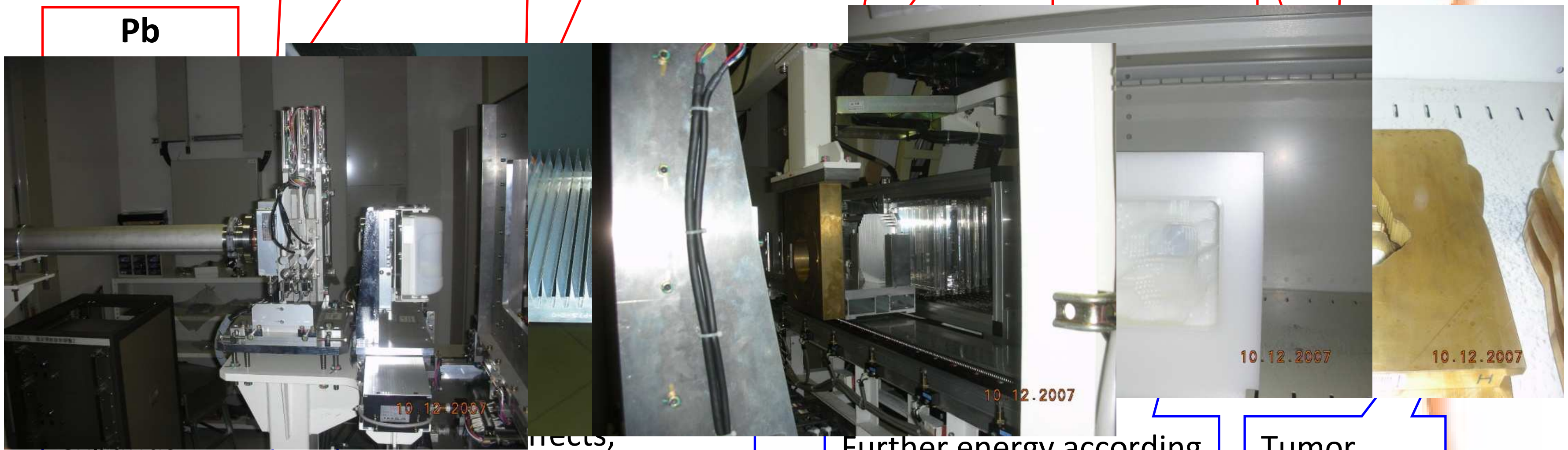
Fine Energy Degrader

Ridge Filter

Ion Chambers

Collimater

Pb



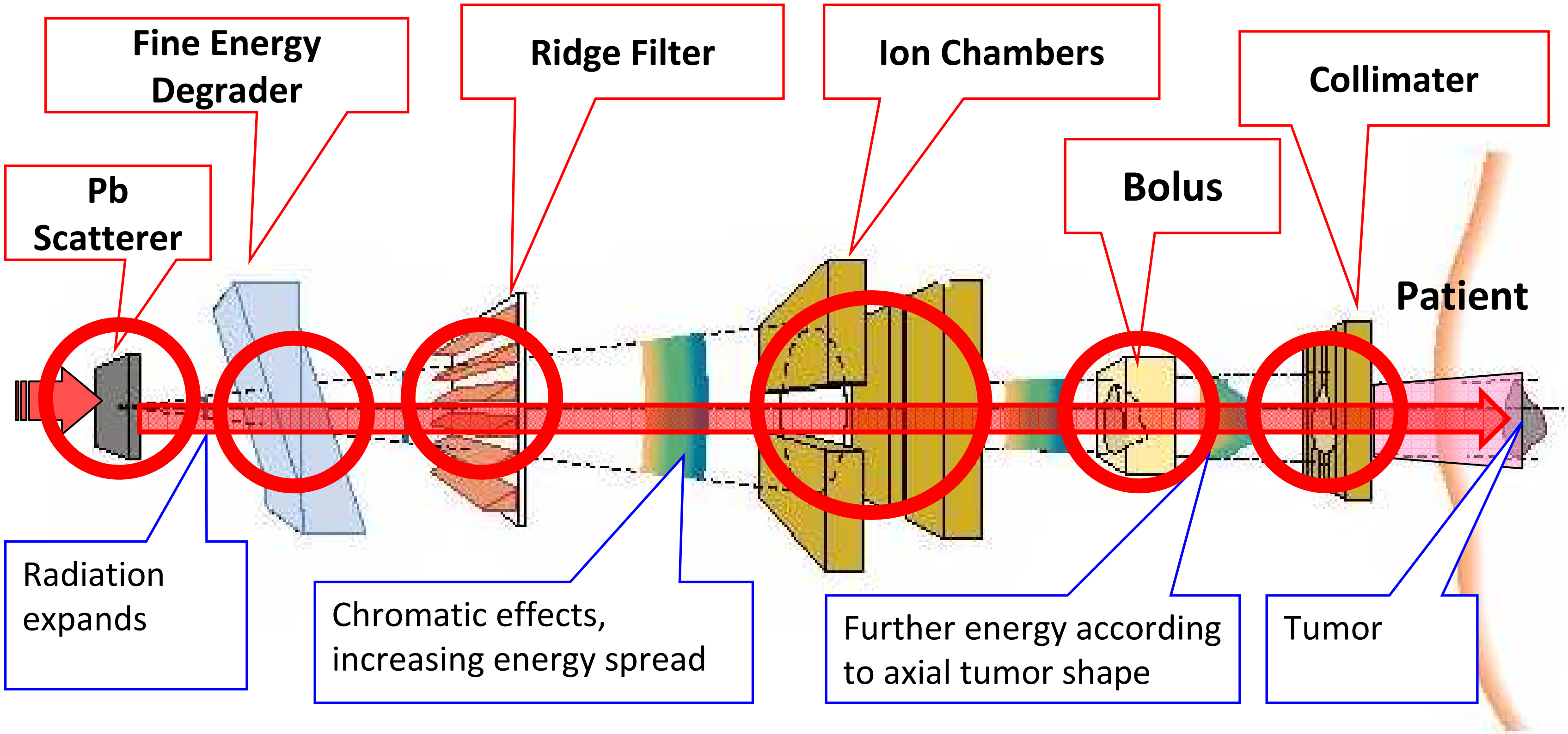
ffects,
increasing energy spread

Further energy according
to axial tumor shape

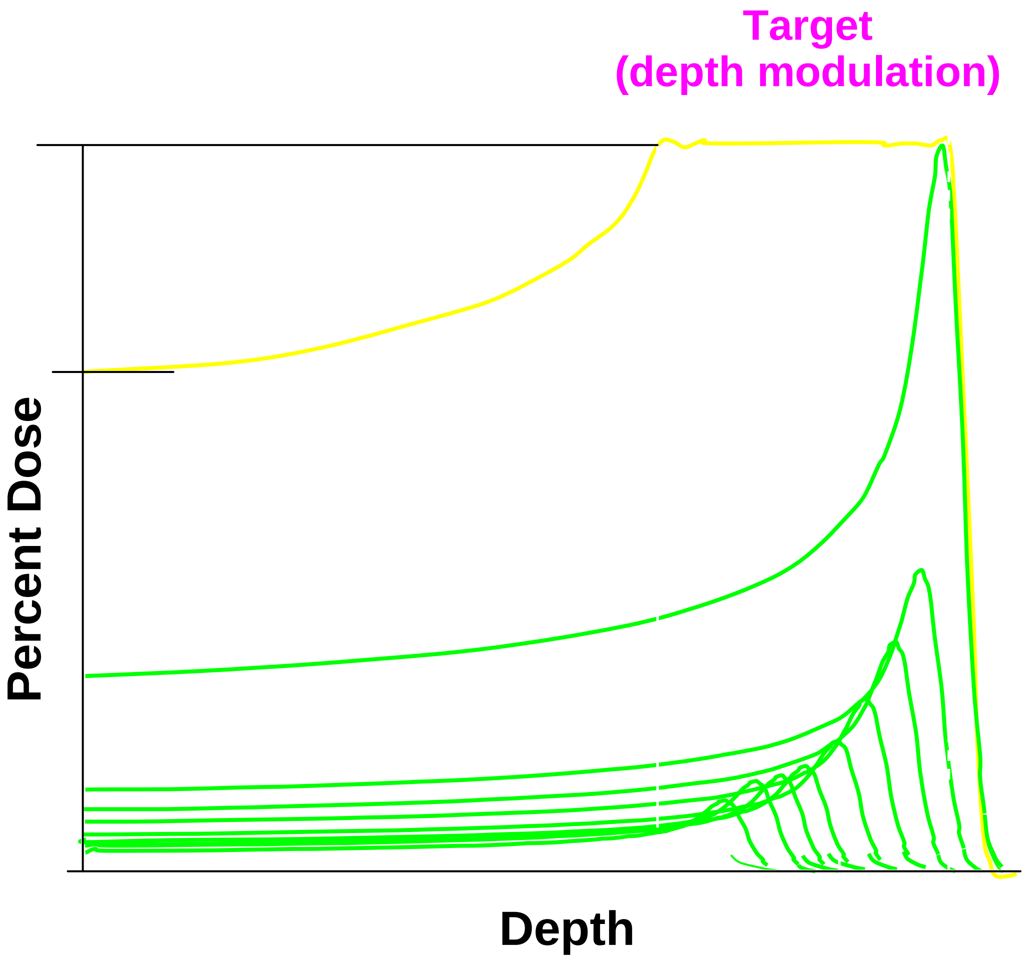
Tumor

Present Systems – passive scanning

- Problem – neutrons and undesired dose on normal tissues

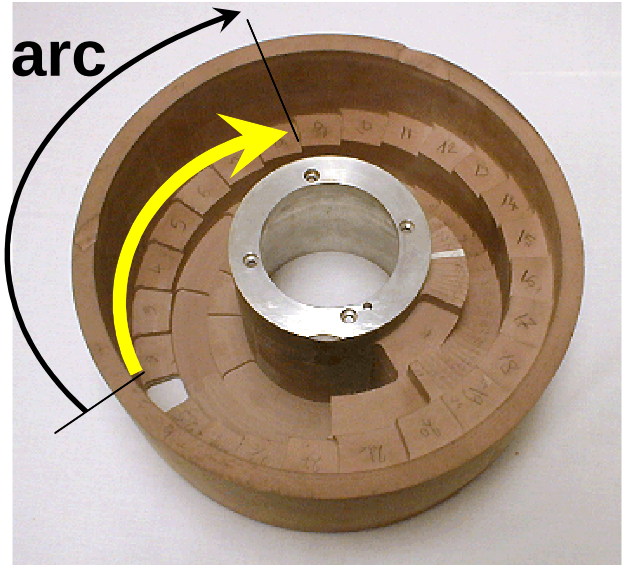


Clinical Proton Beam: The Spread-Out-Bragg-Peak (Passive Scattering)
Low contrast (Compromising of Proton Therapy)



Range Modulator Wheel

- rapidly spinning wheel
- arc = mod



Protom.ru; Protvino, Russia.
Vladimir Balakin.

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- Contacts
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  Phone: +7 (496) 734-17-60
  Fax: +7 (496) 734-19-60
  balakin@protom.ru

The main features of Protom Sync:

- Small dimension (accelerator’s diameter ~5 m) and low power consumption (50 kW for the standard irradiation procedure).
  The complex can be mounted in any existing regional clinic with the oncological division.
  The total area of the required additional building is about 400 square meters (100 square meters of the shielded area);
- Pulse-to-pulse energy changing;
- Slow beam extraction at any energy from 30 to 250 MeV;
- Possibility of upgrading to the energy 330 MeV to provide the regime of proton tomography;
- Controlled beam intensity during the extraction;
- 3-D scanning of the pencil beam;

The main features of Protom Sync:

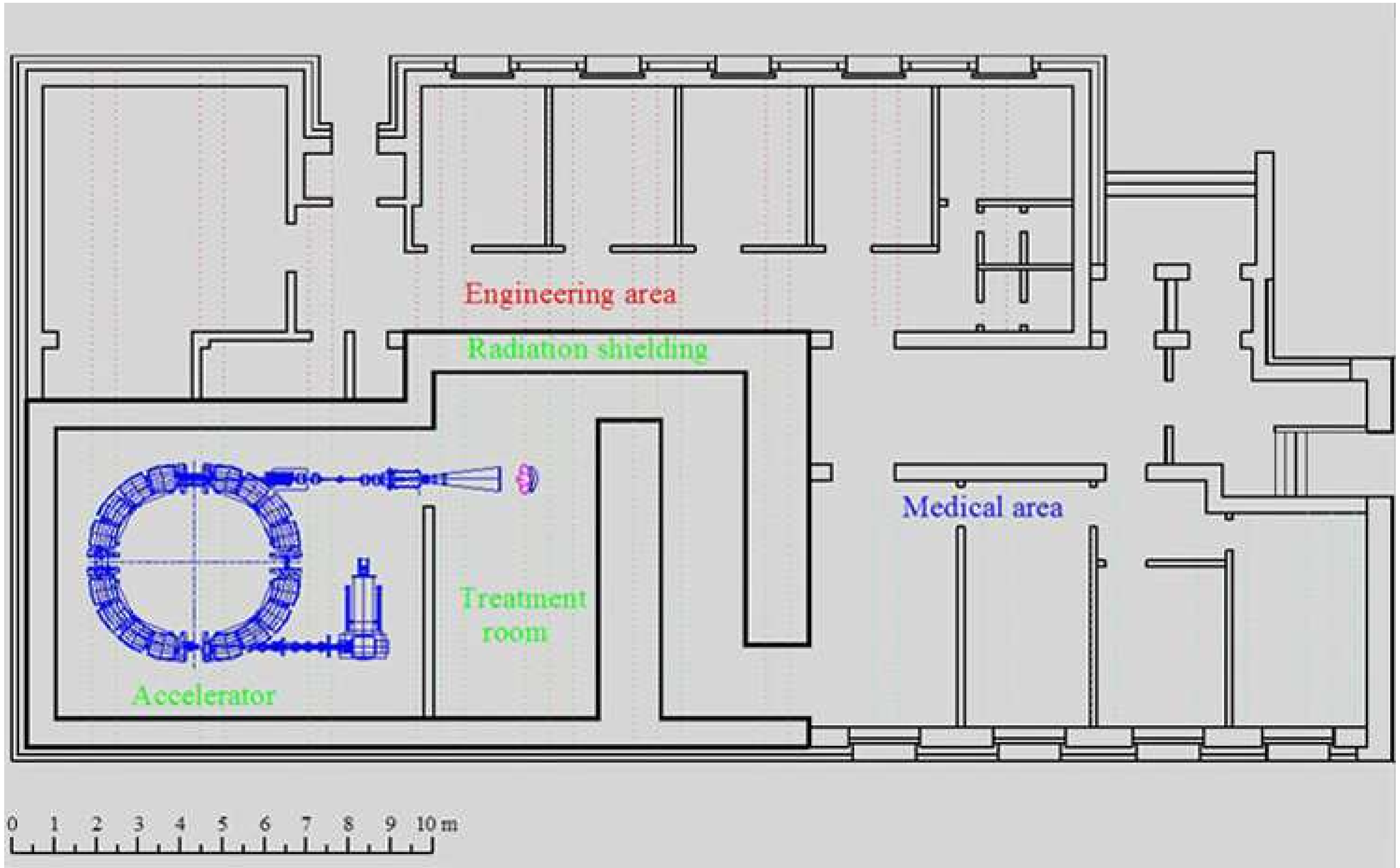
Opportunity: Replacement Market

- Compact, limited-footprint configurations

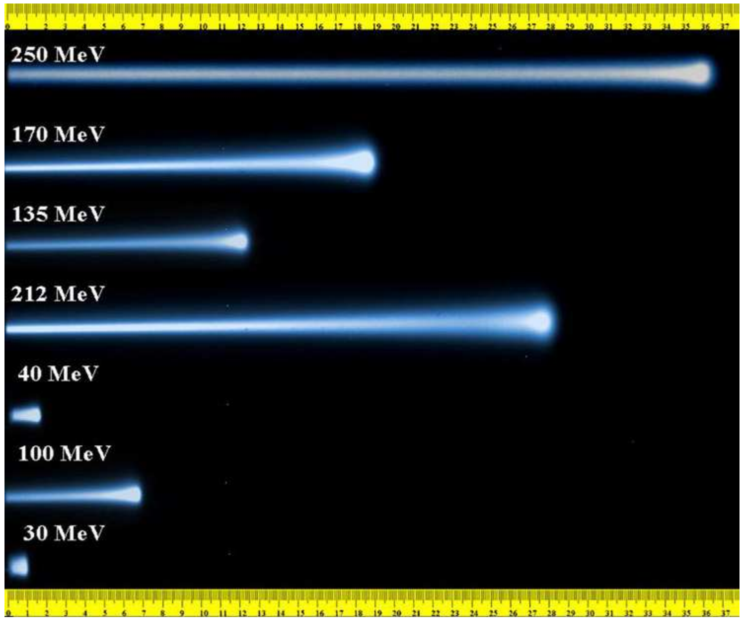
ProTom:
MIT/BINP

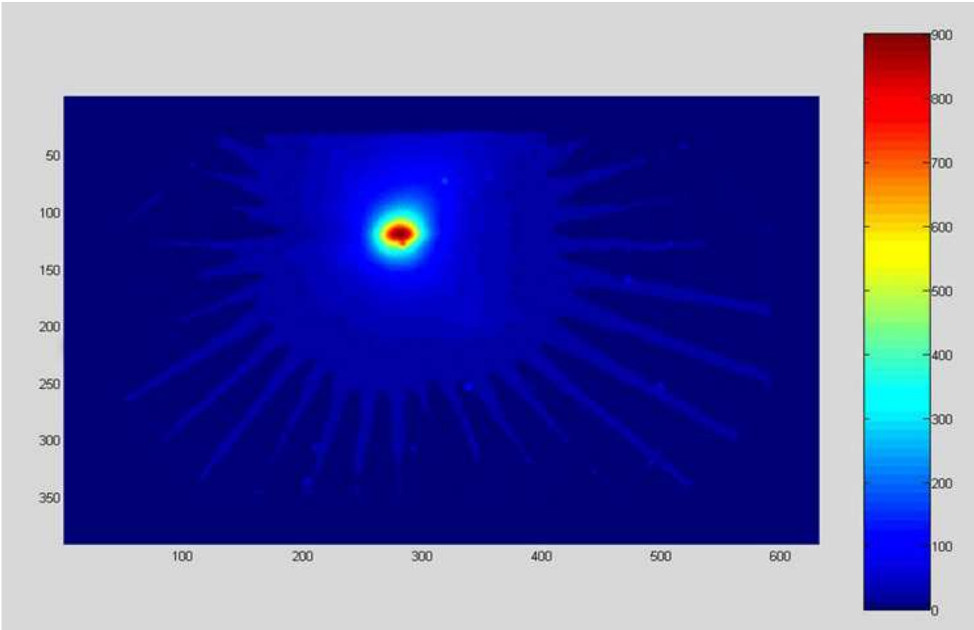
Protom Synchrotron (Radiant 330)

Protom Synchrotron Building



Localized irradiation with Bragg Pick





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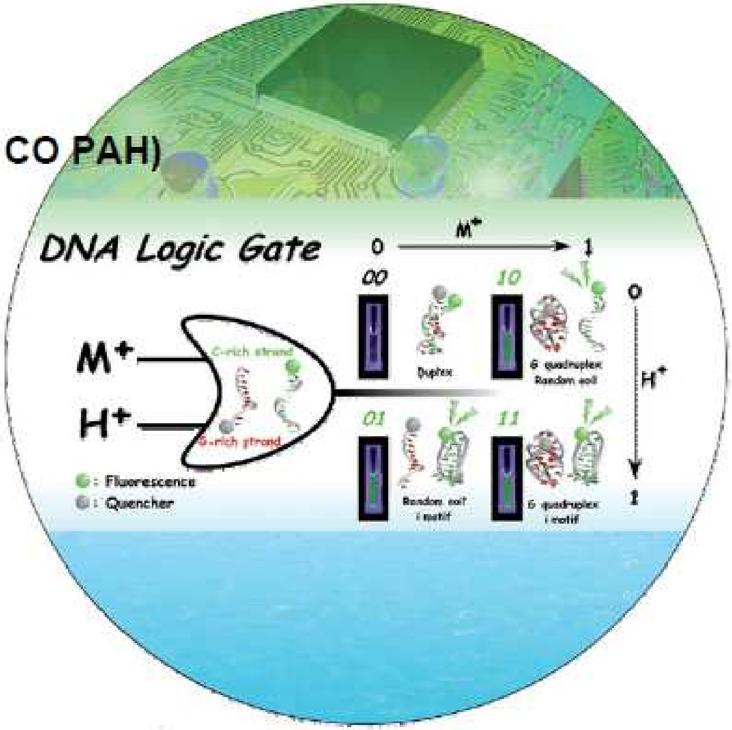


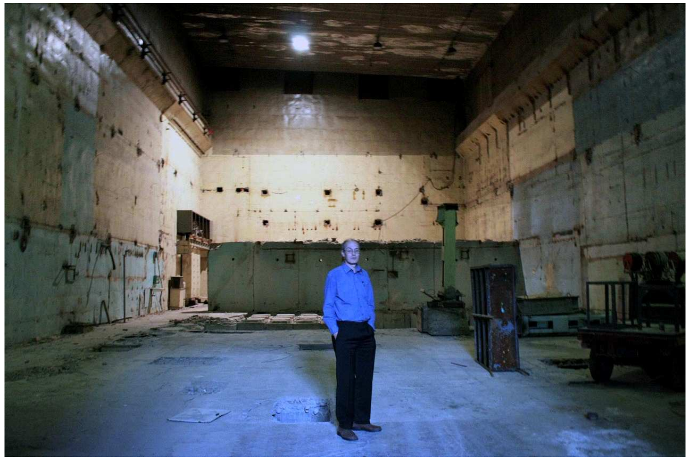
BINP Project Synchrotron

- A lot of vendors propose turn-key systems for proton and ion therapy
- Existing systems forming standards and requirements
- Using of standard design lead to position “in behind back” and patents problem
- Original design causes distrust of customers and many questions
- Strategy is using of world experience and own know-how
- BINP strong sides: electron cooling, superconductive technologies, great experience in design and producing of accelerator systems
- Weak points of standard design: high installation and operation costs, ion gantry, problem of “moving organs” for scanning technique
- Developing of own project and involving to producing elements of standard design

BINP Project

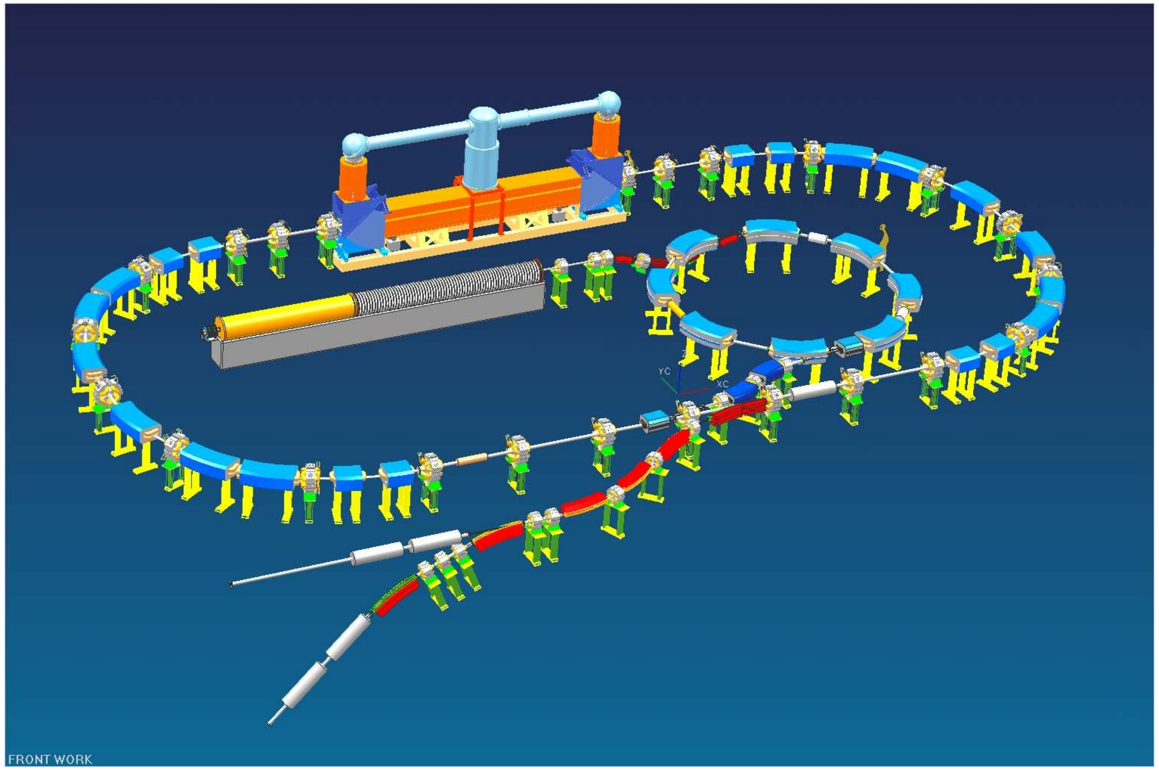
- Problems
- Time to time progress
- Low financial support
- Different level of subsystems development
- No time for R&D
- Customer problems (layout, change of requirements, balance of wishes, technical possibilities and cost)
- Injector (BINP not developed RFQ and ion linac)
- Irradiation system
- Ion TPS
- No medical or med-physical staff
- License and approvals

HITS Activity



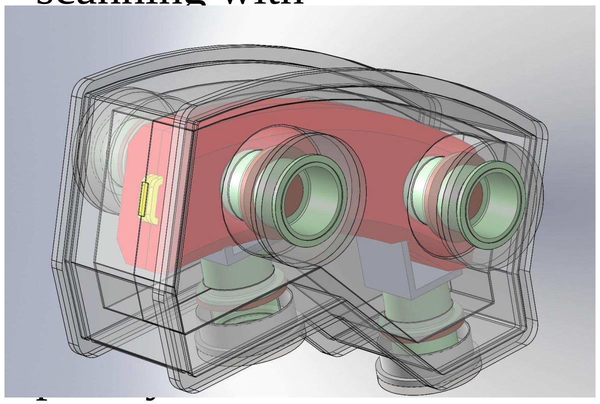
1. General layout, modular structure, proton option
2. Physical design of complex
3. Development of requirements specification for the building and engineering infrastructure
4. Division of responsibility
5. Design of the injector, main elements of booster and main synchrotron
6. Prototypes: ion source, tandem-injector, booster dipole magnet, ferrite kicker, booster electrostatic septum, MR septum, BPM, current monitor, dose monitor
7. Start of preparation of Hall №1 for installation of injector and booster

HITS project of ion therapy facility

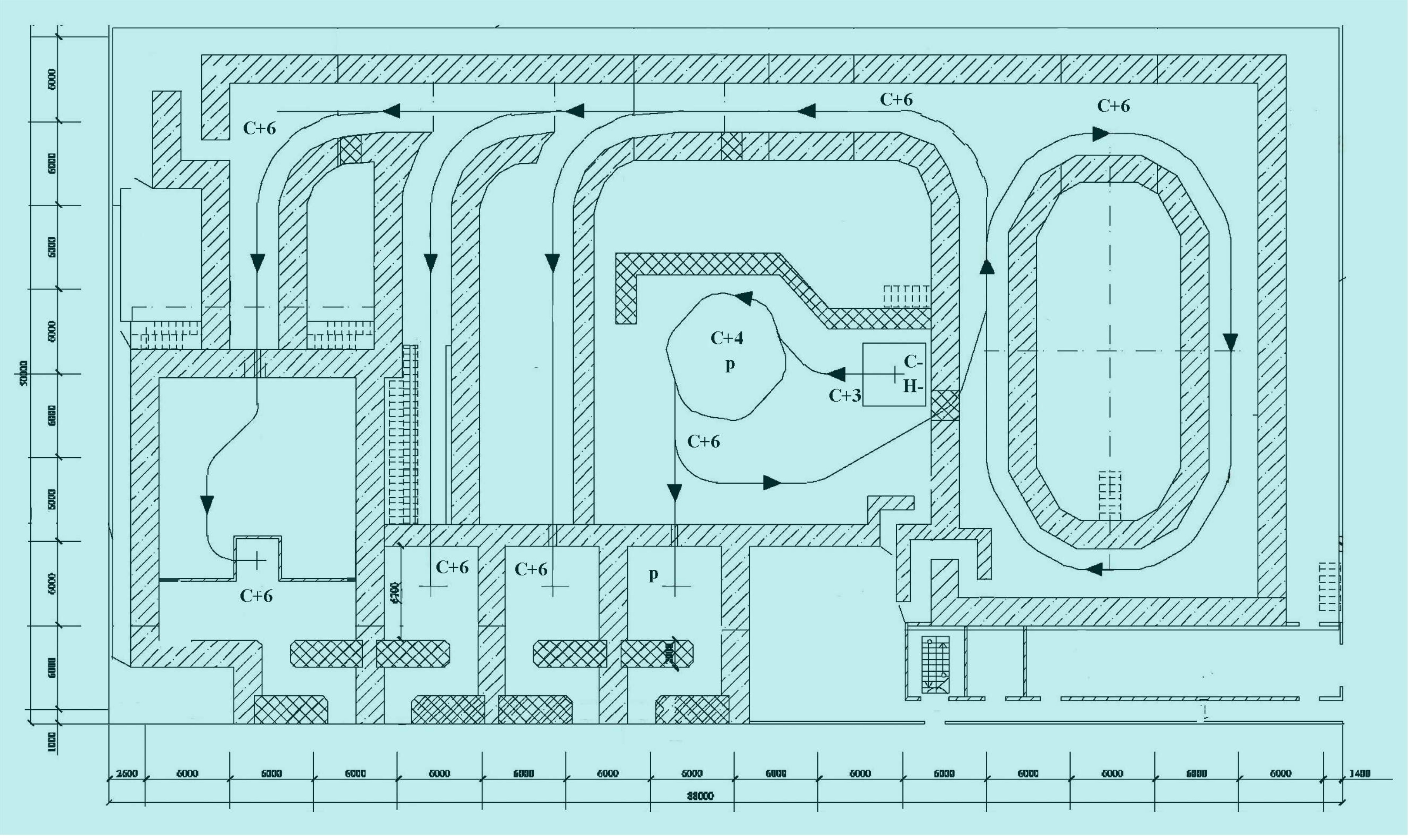


- Racetrack synchrotron with electron cooling
- Booster as source of 250 MeV proton beam for treatment and carbon ion beam 30 MeV/u for injection at main ring
- Accumulation of ion beam at main ring and control emittance for energy range 100-400

- clinical spec: p: fixed ports/gantry, C: fixed ports/ SC gantry
- particle energy: p: 50 – 250 MeV, C: 100 – 430 MeV/u
- average dose rate: 5 Gy/min
- field size: 20 cm × 20 cm
- dose uniformity: ± 4 %
- delivered dose accuracy: ± 2 %
- irradiation method: spot scanning with



HITS Layout



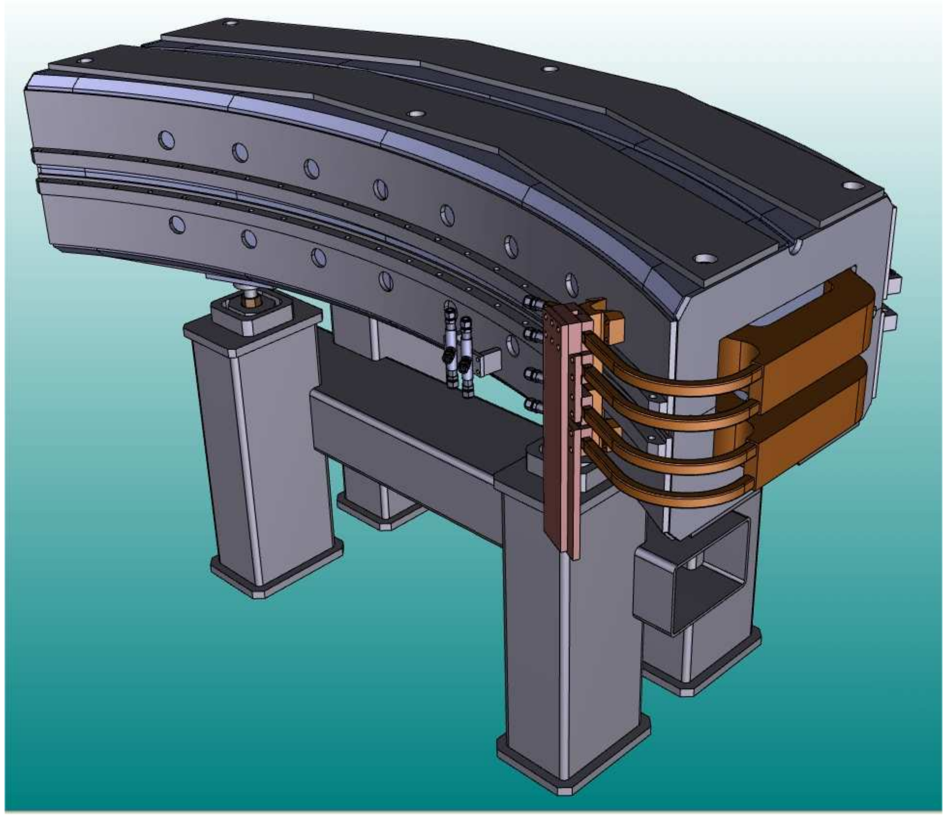
Electron cooling application in therapy facility

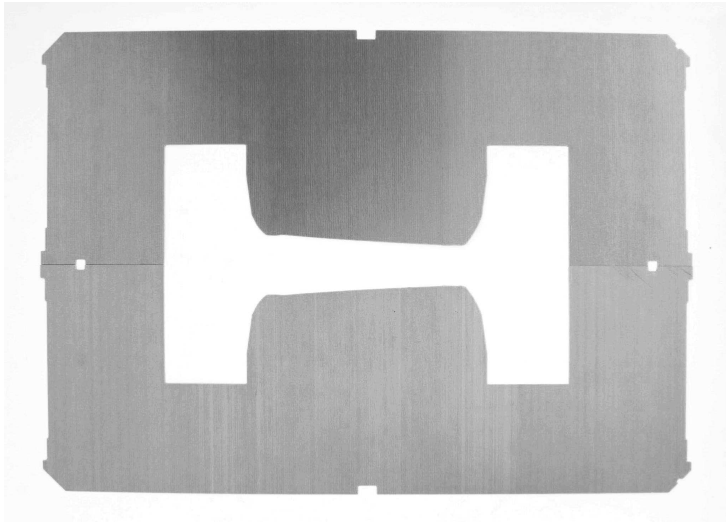
- High intensity of ion beam
- High quality ion beam

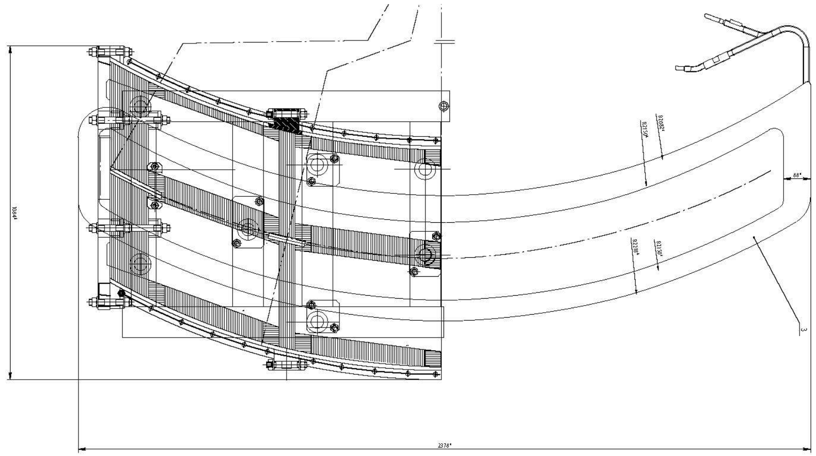
  (extreme small transverse emittance and narrow energy spread)
- Decrease of elements aperture

  (synchrotron & HEBT magnets, gantry, scanners and etc.)
- Precise ion beam energy variation
- Slow extraction on recombination for raster scanning
- Slow small bunches (“pellet”) extraction for spot scanning
- Specific (short-lived PET) isotopes can be accumulated and used for irradiation

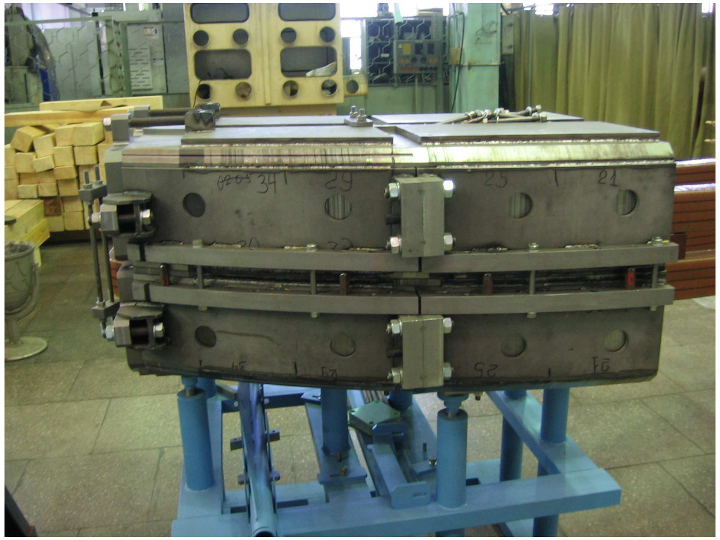
Booster Dipole Magnet



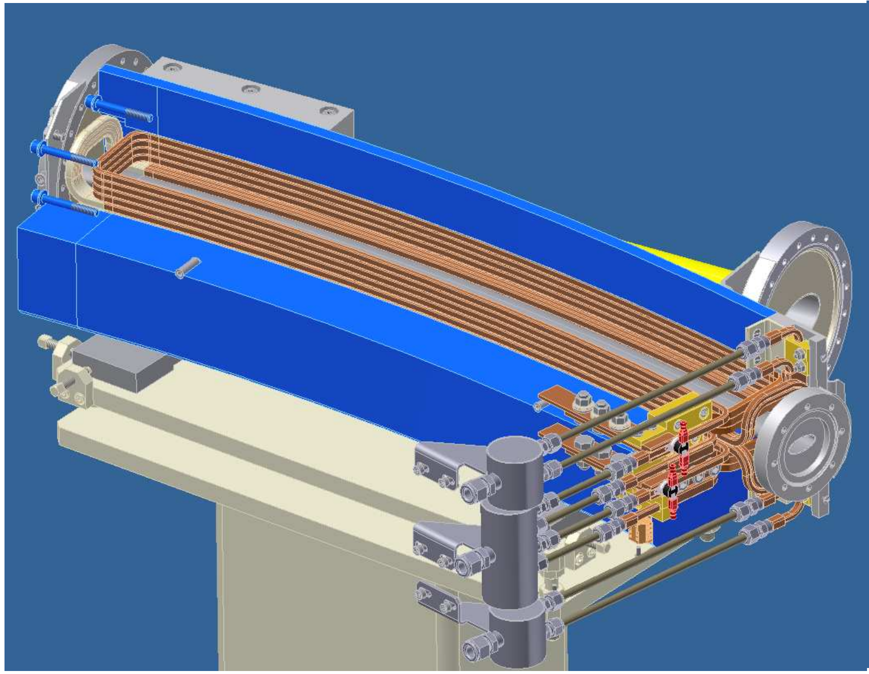


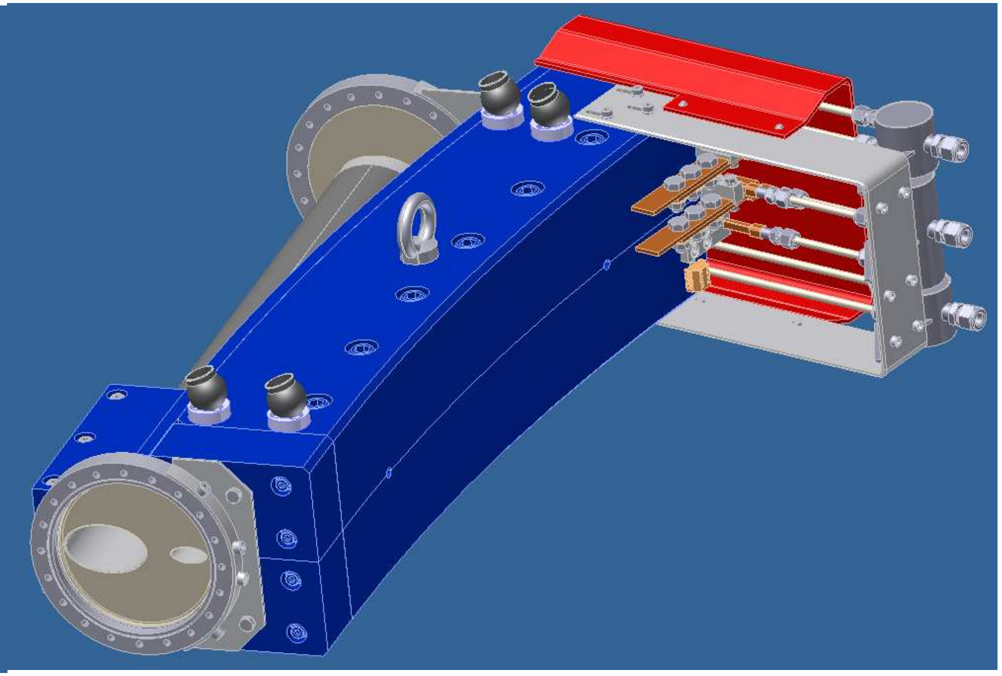


Booster dipole magnet prototype

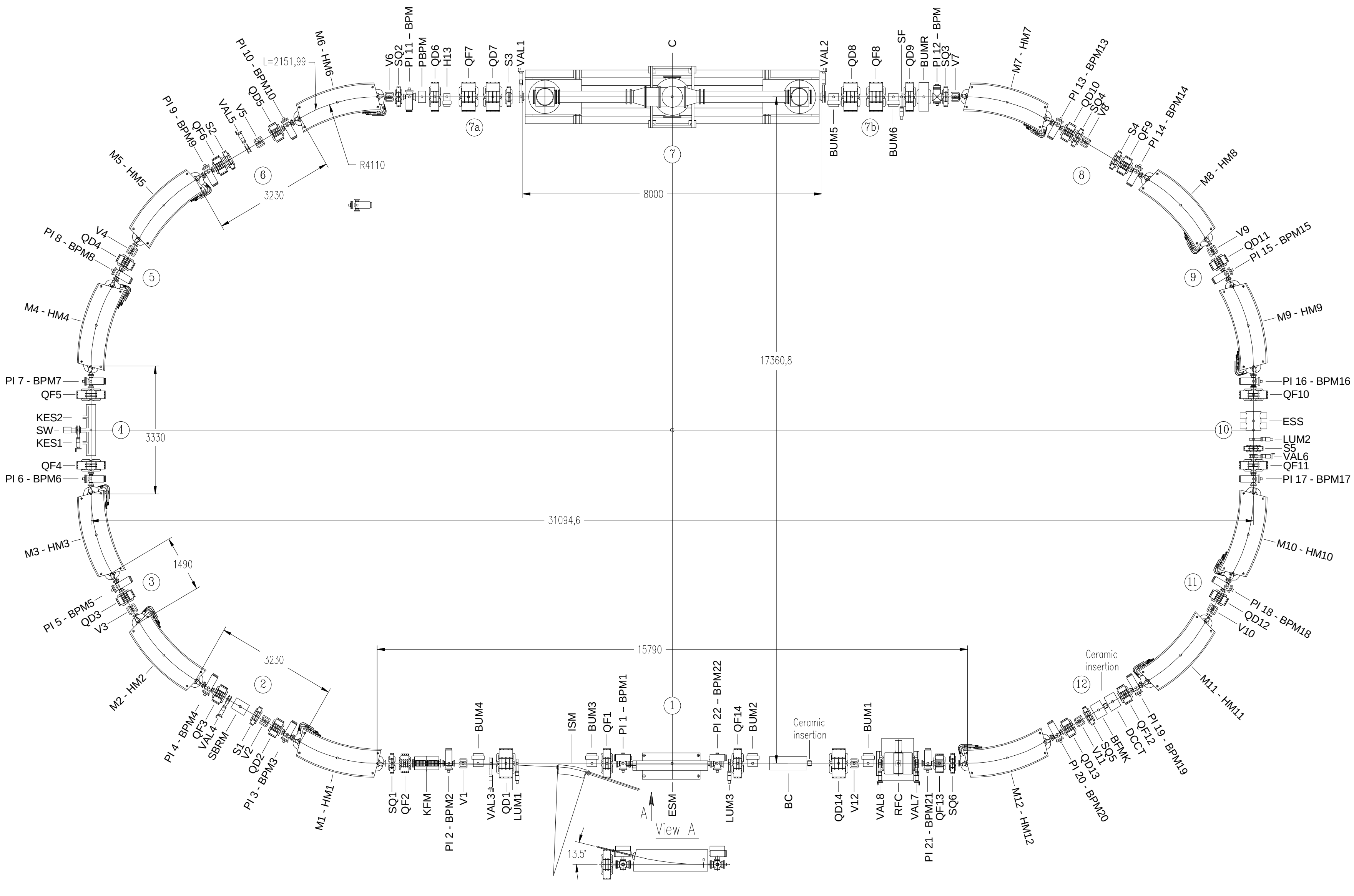


Booster magnet septum





Main Ring



C
8000
17360,8
31094,6
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1490
R4110
L=2151,99
Ceramic insertion
View A
A
13.5°
M1 - HM1
M2 - HM2
M3 - HM3
M4 - HM4
M5 - HM5
M6 - HM6
M7 - HM7
M8 - HM8
M9 - HM9
M10 - HM10
M11 - HM11
M12 - HM12
PI 1 – BPM1
PI 2 - BPM2
PI 3 - BPM3
PI 4 - BPM4
PI 5 - BPM5
PI 6 - BPM6
PI 7 - BPM7
PI 8 - BPM8
PI 9 - BPM9
PI 10 - BPM10
PI 11 – BPM
PI 12 – BPM
PI 13 - BPM13
PI 14 - BPM14
PI 15 - BPM15
PI 16 - BPM16
PI 17 - BPM17
PI 18 - BPM18
PI 19 - BPM19
PI 20 - BPM20
PI 21 - BPM21
PI 22 – BPM22
KES1
KES2
SW
ESS
LUM1
LUM2
LUM3
ISM
ESM
KFM
BC
RFC
SBRM
BFMK
DCCT
PBPM
BUMR
BUM1
BUM2
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BUM4
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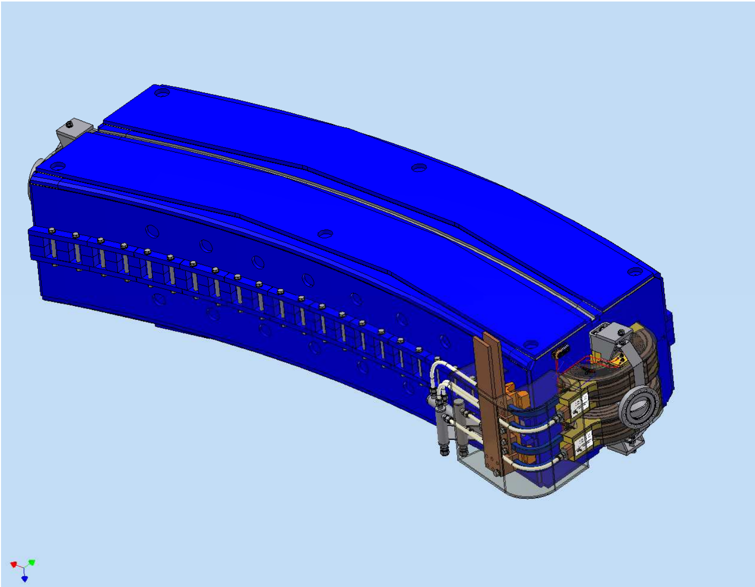
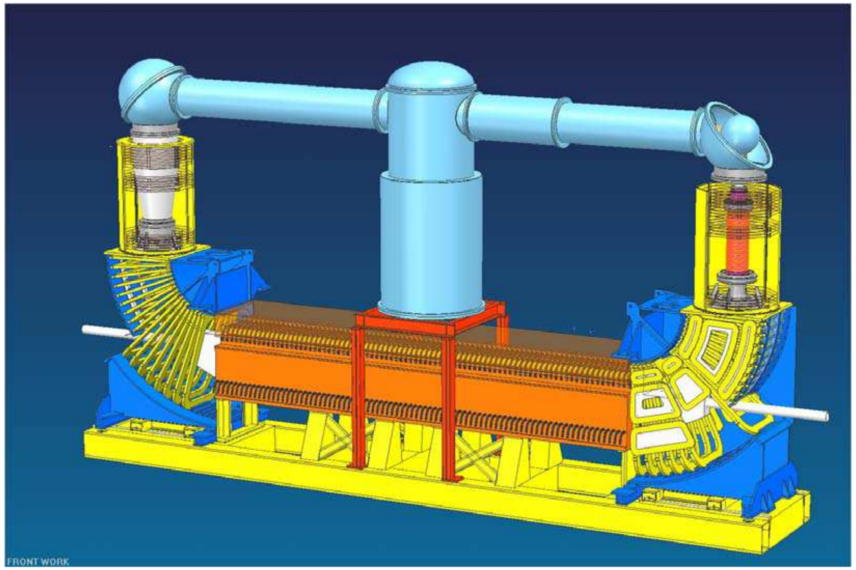
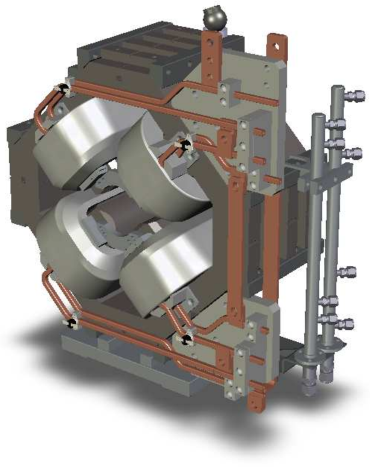
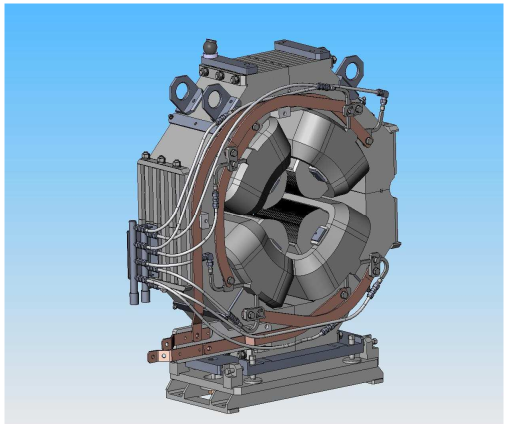
BUM6
SF
H13

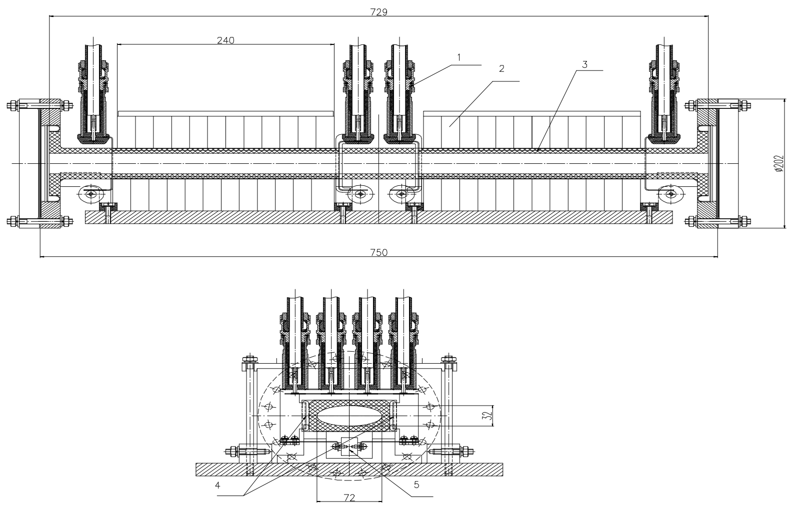
Main Ring Elements



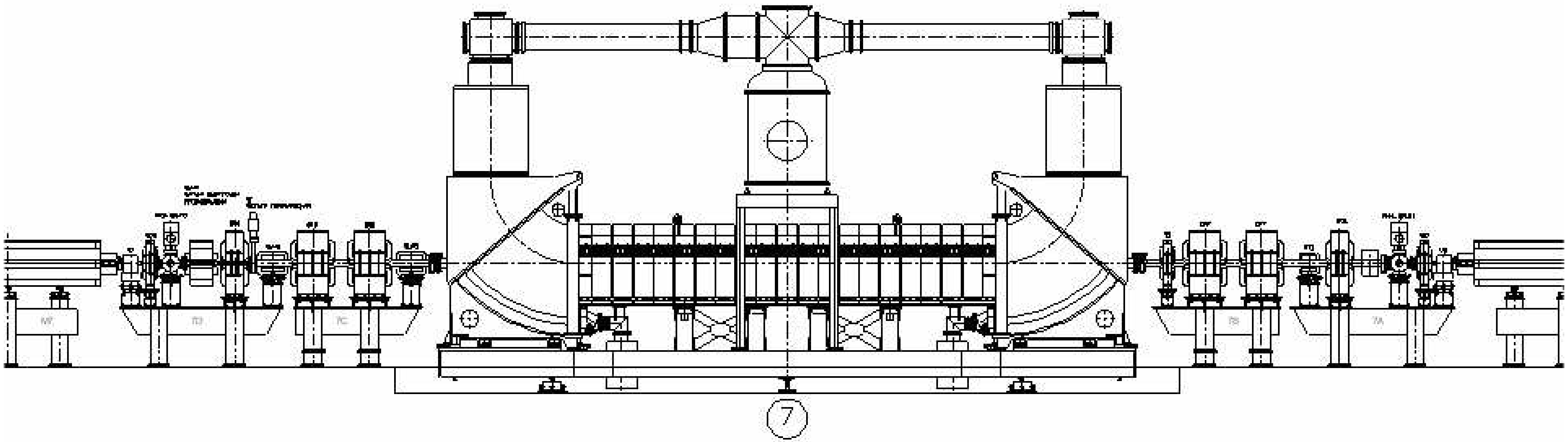


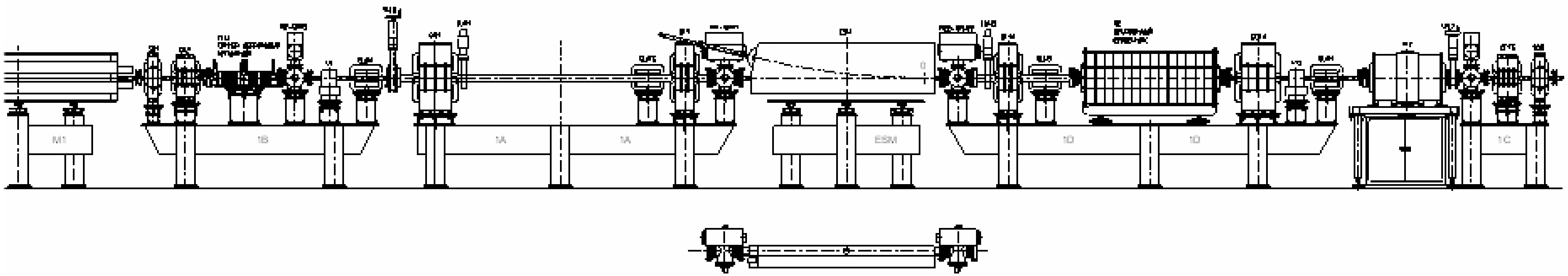






Main Ring, EC & Instrumental drifts





1B 1A ESM 1D 1C

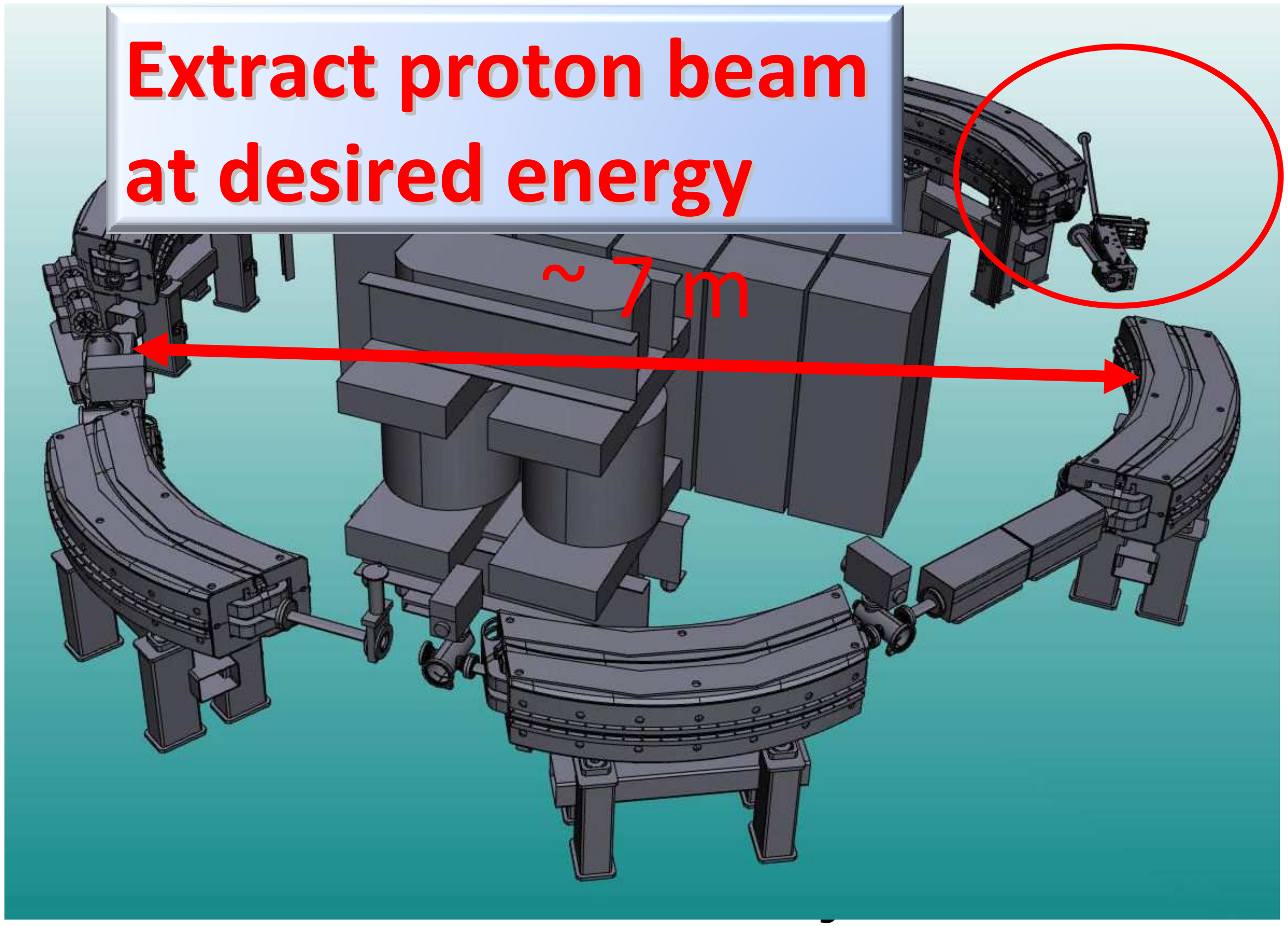
Some problems with the accelerator

- A prototype with required average current does not exist (H^- source, stripping target, breakdowns)
- Energy stability as high as 0.1% (for operation near threshhold)
- Stability of the Li target

New Solutions – Synchrotron

- Synchrotron
  - Minimize background neutron irradiation
- Active Scanning
  - Intensity Modulation Proton Therapy (IMPT)
  - Eliminate neutron emission from passive scatters
  - Lower dose on normal tissues

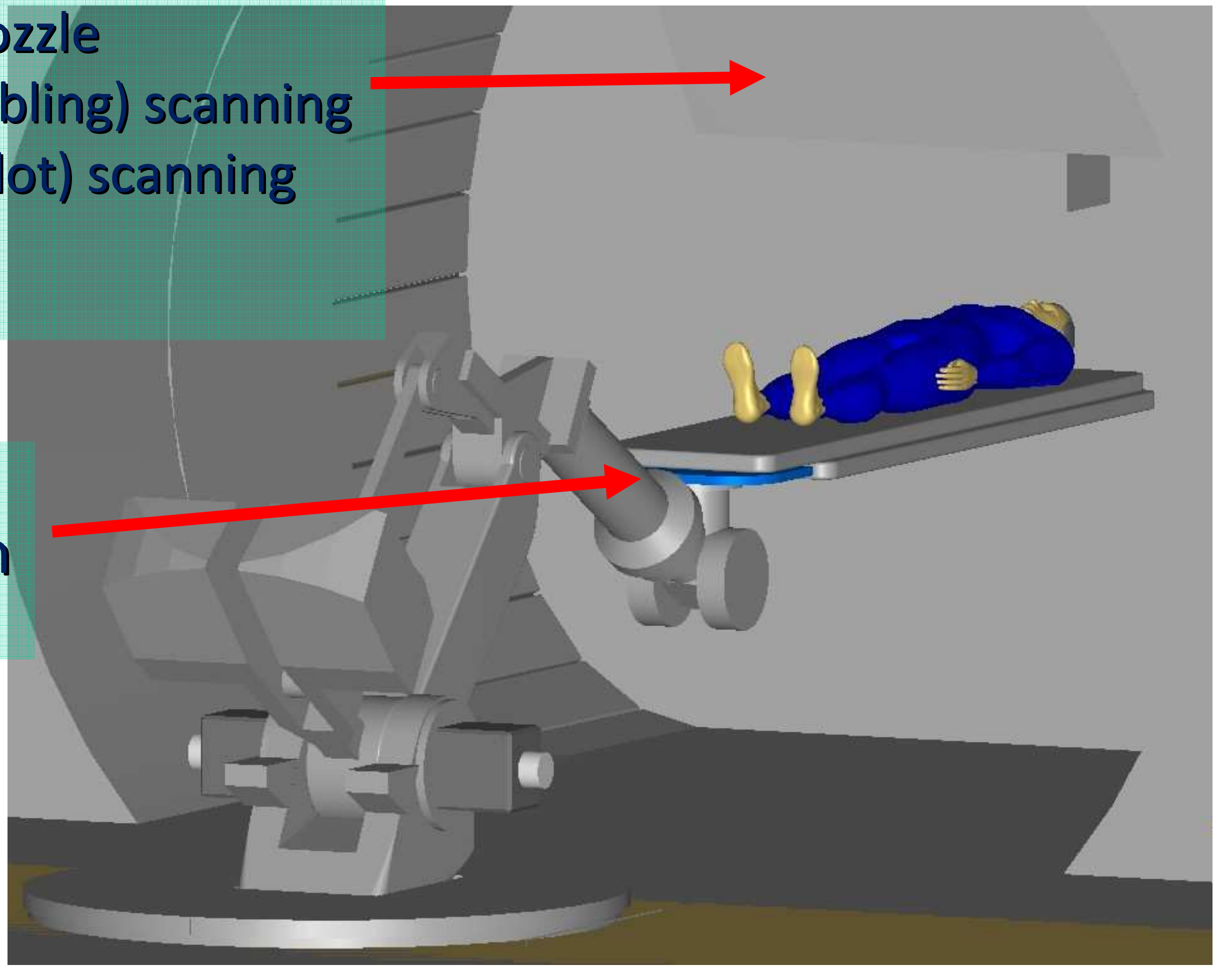
New Solutions – Synchrotron



New Solutions – Treatment Rooms

Active scanning nozzle
- Uniform (Wobbling) scanning
- Pencil beam (dot) scanning
- IMPT

Robotic couch



New Solutions – Synchrotron

	Synchrotron		Cyclotron
	Our Solution-BINP	Others	IBA/SHI/Varian
Energy Range (MeV)	50 ~ 330	Up to 250	250 fixed
Energy Selection	Controlled by synchrotron	Discrete, 4 or 25 steps	Energy degrader + selection system + fine energy degrader at nozzle
Average Dose (Gy/min/liter)	5 Gy	2 Gy	1 Gy
Beam Emittance (mm-mrad)	< 2 π mm-mrad	~ 2 π mm-mrad	> 10 π mm-mrad
Focused Beam Size (mm)	2 mm to 20mm	2mm to 15mm	> 10mm
Capital Cost (US$) 3 gantry rooms + 1 fixed beam room	$45M	~ $65M	~ $58M
Annual O&M Cost (US$ p.a.)	$3M	~ $5M	~ $4.5M
Patient per year Averaged (PTCOG records)	3,000 -	2,000 900 ~ 2,000	1,800 ~ 900
Annual Revenue (US$15,000/patient)	$45M	$10,5M ~ $30M	$10,5M ~ $27M

New Solutions

- High Patient Throughput
  - 3,000 patients per year
- Operation and Maintenance Services
  - Guarantee high system availability
- Physicians and Physicists Training
  - Training programs in USA
- Best Planning System for Proton Therapy
  - New IMPT planning system by MGH

Pulse H^- sources operated

лаборатория/ ускоритель	Тип источника	Скважн, %	ток H^-, мА	Норм.эм., π мм мрад	ресурс, час	Время работы, лет
FNAL, booster	SPS, planotron	0,1	50	0,2 - 0,8 (18 кэВ) 0,8 - 1,5 (750 кэВ)	1000	23
BNL, AGS	SPS, planotron	0,5	75	1,2	4300	19
DESY, HERA	SPS, planotron	0,05	35	1,35 - 0,8	7200	15
PAL, ISIS	SPS, pening	2,5	35	0,3	960	16
PSR	SPS, cusp	10	20	1,3	600	15
KEK, booster	SPS, cusp	0,5		2 (750 кэВ)	1000	15
CERN, RFQ	Volume, cusp	0,75	20	0,5		10
DESY, LinacIII	Volume, cusp		17	0,34	100	4
TRIUMF	Volume, cusp Volume, cusp	100 100	1,9 9	0,15 0,5	большой 300	23 6

Distribution of responsibilities

H^- source	Initial acceleration, beam transport, diagnostics	Stripping target	Accelerator	High energy beam line	Neutron producing target
10 mA, 25 kV: Bel'chenko 50 mA: Dimov	120 kV, H^-, H^+, O^+ Kudryavtsev, Konstantinov Khilchenko Tiunov	Davydenko Krivenko	Shirokov Sorokin Kandaurov Salimov Nemytov	Davydenko Medvedko	Taskaev Bayanov Maximov

Stripping target

Длина $L \approx 40$ см

Внутренний радиус $a \approx 0.5$ см

Плотность Ar $n \approx 8 \cdot 10^{14}$ см$^{-3}$

Энергия ионов H^- $E_b \approx 1$ МэВ

Ток ионов H^- $I_b \approx 10$ мА

ПРОБЛЕМЫ

1. Потери энергии пучка и ионизация мишени: $\Delta E \approx 600$ эВ, A=18 ионизаций, плотность плазмы $n_i \approx \dfrac{AI_b}{\pi a L v_i} \approx 3 \cdot 10^{10}\, см^{-3}$

2. Потоки газа, ионов, электронов и ультрафиолета: фотоны $S \approx 30\ I_b \approx 2?10^{18}$ с$^{-1}$, поток фотоэлектронов в ускоритель - $I_p \approx \gamma\, S < \Omega >$, при $\gamma \approx 0.1$ - $I_p \approx 80$ мкА

ISTC project # 1484: main results

- Electrical strength and leak currents were studied with a prototype
- High voltage power supply was tested at 1.4MV
- Bunker with shield was prepared
- Conceptual studied of different versions of stripping target were completed
- A prototype of H^- ion source with 5mA current was developed

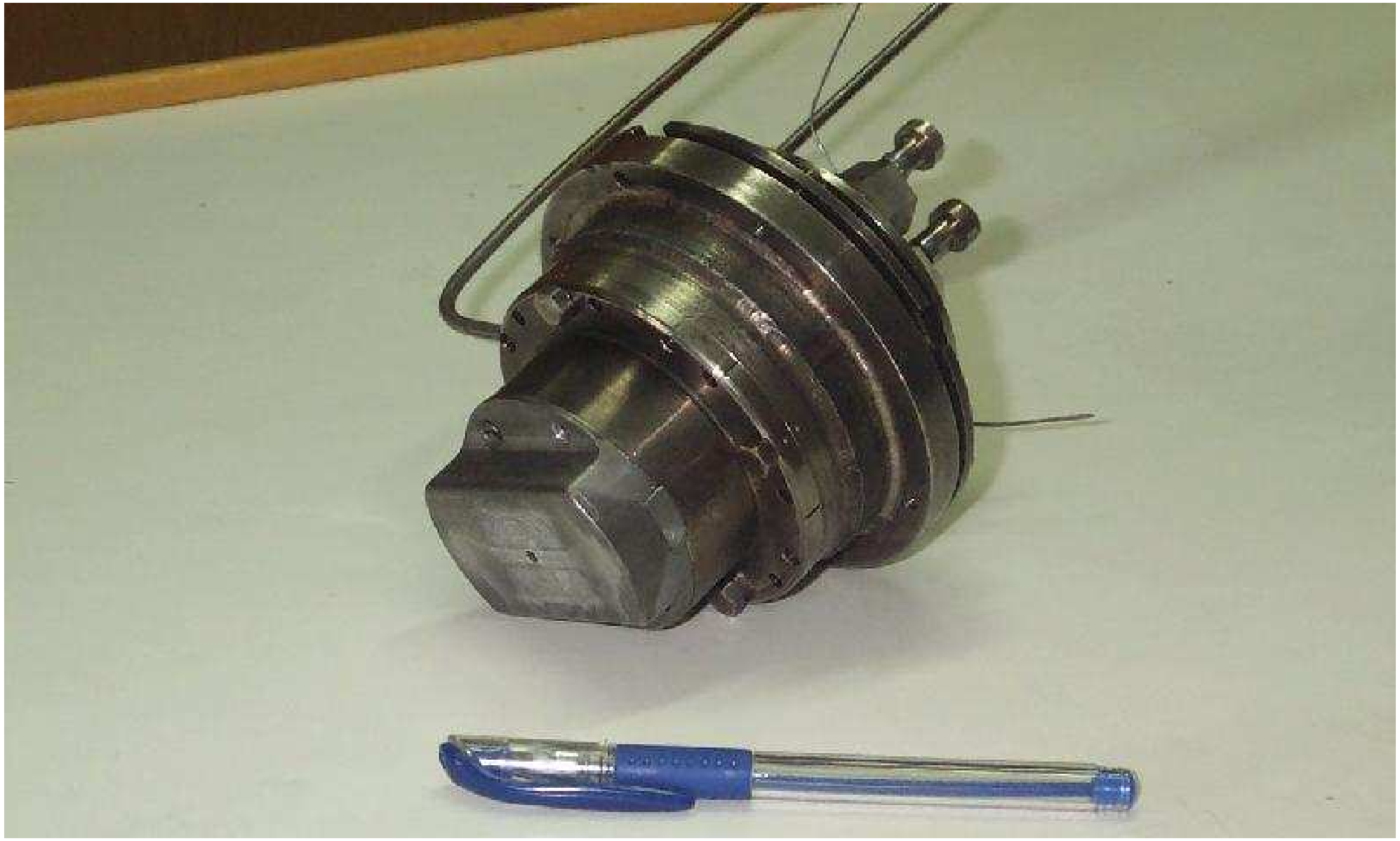
- Development of 50 mA ion source has been started
- Numerical simulations of beam transport were completed
- Energy stabilization methods were considered
- Several versions of neutron generating target were considered
- Neutron field was numerically simulated

Major objectives of new ISTC project

- **Task 1. Production of negative ion beam**
- **Task 2. Production of accelerated proton beam (2MeV energy)**
- **Task 3. Neutron production**

High voltage power supply (ELV accelerator)

Prototype of negative ion source



Conclusions

- Conceptual design is completed in the scope of ISTC project #1484
- ISTC projet #2569 has been started in November 2003
- **Neutron production is Demonstrated on a target**