



Particle Therapy: project status for St. Petersburg

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e The workshop on “Ions for cancer therapy, space research and material science”, Chania, Crete, 28-August, 15:45 - 16:15Greece

<https://indico.cern.ch/event/559908/>

Particle Therapy:
project status for St. Petersburg

Abstract

The main ideas of the Centre of Hadron Therapy and Diagnostics of Oncology Diseases for the North-West Region of RF are represented in the general context of the developments and current trends in particle therapy in Russia and in Saint-Petersburg. The experience and the outlook could be useful for planning of the newly emerging centers.



Layout:

- **Introduction. The goal is to share the experience. Brief history.**
- **Oncology deceases in Russia and tendencies**
- **Proton centers at research scientific institutions of RF**
 - JINR
 - ITEP
 - PNPI (Gatchina)
 - INR (Troisk)
- **Proton medical centers under construction**
 - Dimitrovgrad
 - Obninsk
 - R&D for Carbon ions in IHEP(Protvino)
- **Nuclear Medicine cluster in the Southern Urals in the Russian Federation**
- **Status of Nuclear Medicine in Saint-Petersburg region**
 - Proton therapy medical center (commercial)
 - Proton PNPI ophthalmology
 - Radium Institute
- Saint-Petersburg state university –Education, research and outreach
- Summary

North-West district of RF



Administrative center

- Saint-Petersburg

Area

• Total 1,687,000 km² (651,000 sq .m)

Population (2010)

• Total 13,616,057

<https://en.wikipedia.org/wiki/Russia>

The Project for the Center of Hadron Therapy and Diagnostics of Oncology Deceases for the North-West Region of RF was initiated by the SPbSU in 2003

Participants– leading Saint-Petersburg institutions, coordinated by the SPbSU :



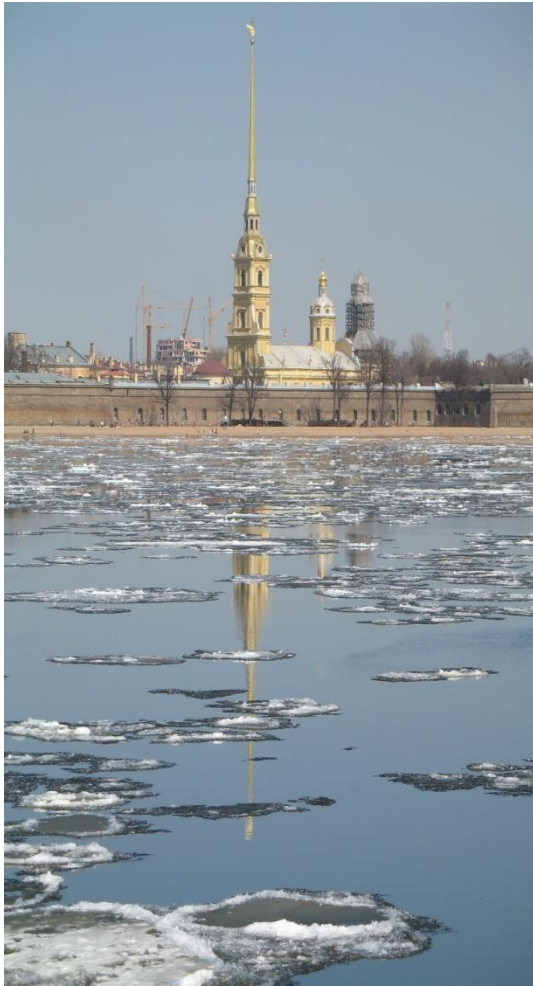
- V.A.Fock Institute of Physics of Saint-Petersburg State University ([SPbSU](#), Ministry of Education, RF)
- Federal State Unitary Enterprise “D.V. Efremov Sci.Res. Inst. of Electrophysical apparatus” ([FSUE NIEFA](#), MinAtom)
- Central Design Bureau of machine Building ([CDBM](#), MinAtom RF)
- St.Petersburg City Clinical Oncology Centre ([SPbCCOC](#), St.Petersburg Health Protection Committee)
- Central Research Institute of Roentgenology and Radiology, SPb ([CRIRR](#))
- Petersburg Nuclear Physics Institute named after B.P.Konstantinov ([PNPI](#), RAS, Gatchina)
- Research Institute of Hygiene, Occupational Pathology and Human Ecology ([RIHOPHE](#), Federal Bureau of Medical and Biological Extreme Problems, the Ministry of Health of Russian Federation)

The goal of the Project:

to develop the new medical facility –
the Centre of Hadron Therapy and Diagnostics of Oncology Diseases
for the North-West Region of RF

- Protons and carbon ions -- PIMMS as a baseline solution
- The newest methods of screening and diagnostic of oncology diseases
 - a network of nuclear diagnostic medicine laboratories (PET, SPECT, MRI) in the North-West Region
 - early diagnostics
 - digital mammography and fluorography mass screening
 - electronic medical cards
 - information technologies based on the distributed data analysis in mass scale diagnostic systems
- Consortium of specialists from leading Saint-Petersburg institutions
- In contact with ENLIGHT community
- **Strong scientific and educational components**

Major ideas of St.Petersburg hadron therapy project :



1. To start from the burning issue for the region – from the urgent upgrade of the existing conventional X-ray therapy and radioisotope diagnostics facilities in Saint-Petersburg (including also medical cyclotrons for radionuclide production, farm.labs, SPECTs, etc.). Completion of 80 MeV cyclotron at PNPI for the eye tumor treatment.
2. A turn-key facility for p- and ^{12}C - hadron therapy integrated into the existing infrastructure in Pesochniy (that includes the municipal hospital for 600 patients, the Oncology Institute and CRIRR).
3. Implementation of GRID as a major information platform for all diagnostic networks including the X-ray chest screening examinations in the North-West region of RF, digital mammography and SPECT data, introduction of the electronic cards for all patients, – in order to ensure the early efficient diagnostics and patient selection
4. Strong educational and research components in collaboration with European centers (ENLIGHT++)

→ see further...

Introduction. A bit of history...



- **March 2003** –the 1st discussion with M.Regler at CERN
- **11.06.03** the 1st meeting of the initiative group of 7 leading institutions of St.Petersburg
- **2004**, the ISTC project #2887 on the development of technical proposals for HT in SPb was ...“accepted without funding” ...
- **2006 March-October** – a new round of preparations of the official letters and documents in St.Petersburg was stipulated by the ENLIGHT++ meeting in March 2006
- **November 2006**, Letter was signed by the Major of St.Petersburg and sent to the Ministry of Health of RF asking for approval and the Federal support


To the Minister of Health
and social development
the Russian Federation
M.Yu.Zurabovu

20.11.2006

“.....Due to the above mentioned arguments I would like to ask you to consider the inclusion the North –West Interregional Center for Hadron Therapy into the national priority project “The Health“, the section "Oncology ".

In St. Petersburg there exists large intellectual and technological capabilities of physicists and engineers working in the field of radiation technologies, which allows, in the case of a positive decision, to use the potential of the city for the creation of this center with the application of the latest achievements and developments of the scientists. “

Sincerely, The Major St. Petersburg
V.I.Matvienko “


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САНКТ-ПЕТЕРБУРГА
Сеймад, Санкт-Петербург, 191060
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E-mail: gov@spb.ru
http://www.gov.spb.ru

20.11.06 № 04-115/9417

На № _____ от _____

Министру здравоохранения
и социального развития
Российской Федерации

М.Ю.Зурабову

Уважаемый Михаил Юрьевич!

На сегодняшний день Санкт-Петербург занимает второе место в России по количеству больных онкологическими заболеваниями. Методика лучевого лечения злокачественных опухолей является основным инструментом современной онкологии. В среднем по России лучевое лечение получают около 30% пациентов. При этом в Санкт-Петербурге данный показатель не превышает 15-20%.

Одним из новых направлений в развитии лучевых высокотехнологичных методов лечения онкологических заболеваний является адронная терапия. По оценкам ученых Санкт-Петербурга, данный метод лучевой терапии, несмотря на малое распространение в Европе, уже показал перспективность и имеет тенденцию развития в обозримом будущем.

В связи с вышесказанным прошу Вас рассмотреть вопрос о включении в приоритетный национальный проект «Здоровье», раздел «Онкология» организацию Северо-Западного межрегионального Центра адронной терапии.

В Санкт-Петербурге имеются большие интеллектуальные и технологические возможности физиков и инженеров, работающих в области лучевых технологий, что позволяет, в случае положительного решения, использовать потенциал города для создания указанного центра с внедрением самых современных достижений и наработок ученых.

Губернатор
Санкт-Петербурга

С. Шансисен
В.И. Матвиенко

В.И.Матвиенко

Правительство Санкт-Петербурга
Комитет по здравоохранению
Вход № 01117-364700200
от 22.11.2006

Introduction. A bit of history...



- **January 2007** – **the positive reply is received from Moscow...**
- **02 March 2007**, “**Medical and Technical Justification of the North-West Centre of High-Tech Therapy of Oncology Deceases**” were submitted to the Health Committee of St.Petersburg
- ...
- **2008: Proposals** to the SPb Health Committee -- for **Fluo-GRID-** and **Mammo-GRID** pilot prototype developments ...
- **2008: Proposals** for the upgrade of **PNPI** medical beams ...
- **2009: Proposals** for **Child oncology Proton Therapy Center** in **SPb...**
- 2011 – the project of the North-West Centre of Hadron Therapy is still frozen...-- *the protocol on the commercial Proton therapy center with MBIS private company was signed instead*
- **2013:** **polytical decisions** are taken for **proton 80 MeV cyclotron** at **PNPI (Gatchina)** for the **eye tumors treatment...**
- **2015, October**, **The Road Map for Nuclear medicine in RF**
- **2016: Proposal** of the North-West Centre of Hadron Therapy was submitted **to Strategy -2030 Pogram of SPb development...**
→ **see further...**

“Number of patients potentially eligible for proton therapy”

Bengt Glimelius, Anders Ask, et al. Acta Oncologica

Volume 44, 2005 - Issue 8 Pages 836-849

Sweden

...due to the obvious benefits of protons “... *the potential number of patients is the same as the majority of patients treated with external radiation therapy.*”

...

“Thus we find that this Swedish study and three separate other European investigations, having very different designs, reach the conclusion that between 13–16% of all irradiated patients are suitable for proton therapy”.

- For Saint-Petersburg region : ~ 20 000 cases each year
- > 10 000 patients – for beam therapy (the WHO indicates ~ 70 %)
- About 1300-1600 patients – for proton therapy

Cancer treatment methods in St.Petersburg region in 2007 [1]

8784 patients in SPb in 2007[1]

	Russian Federation	Moscow	St.Petersburg
Surgery(only)	45%	57,5	61.1%
Beam therapy (only)	14.5%	6.1%	4,8%
Drugs(only)	5.3%	5.2%	4.4%
Combined/complex	32.6%	30.3%	27.8
Chemo+Beam	2.7%	0.9%	1.9%

...very high level of surgical methods in SPb,

very low level of beam therapy..

[1]. Мерабишвили В. М. Онкологическая служба в Санкт-Петербурге и районах города в 2007 году. Ежегодник Популяционного ракового регистра. - СПб., 2008. - С. 44-47.)

2007: Cancer mortality rates in Russia regions[1]

Region of RF	Mortality (men, per 100 000)	Place amongst regions of RF	Mortality (women, per 100 000)	Place amongst regions of RF
Ярославская обл.	270,76	16	205,52	6
Ивановская обл.	275,16	11	189,54	12
Липецкая обл.	239,48	37	153,78	54
Архангельская обл.	230,24	46	164,35	36
Самарская обл.	229,35	47	158,20	49
Астраханская обл.	235,53	41	158,40	47
Свердловская обл.	243,94	33	173,06	26
Новосибирская обл.	271,30	13	175,44	23
Алтайский край,	259,70	25	163,79	38
Республика Татарстан	200,09	58	142,18	63
Башкортостан.	178,34	67	120,31	70
Saint-Petersburg	289,49	5	263,09	1
РОССИЯ	231,54	-	171,16	-

[1]. Мерабишвили В. М. Онкологическая служба в Санкт-Петербурге и районах города в 2007 году. Ежегодник Популяционного ракового регистра. - СПб., 2008. - С. 44-47.)

Oncological Statistics for Russian Federation in 2016:

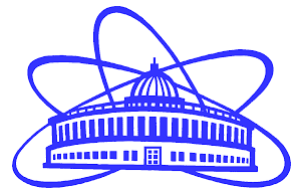
- Oncology – takes the 2nd place in mortality in RF -- **15,6%**. [1]
- **3,5 mln** oncological patients in Russian Federation [1]
- **More than 500 000** new cases each year [1]

The current population of **the Russian Federation** is **143,366,997** as of Tuesday, August 15, 2017, based on the latest United Nations estimates.
<http://www.worldometers.info/world-population/russia-population/>

[1] <https://ria.ru/society/20170710/1498235244.html>

[2] **V.M. Merabishvili** Oncological Statistics (traditional methods, new information technologies). Guidelines for physicians. Second edition, supplemented. Part I. — SPb., 2015. — 223 p.

Proton centers at research scientific institutions -- JINR



http://mtk.jinr.ru/index.php?option=com_content&task=blogsection&id=4&Itemid=39

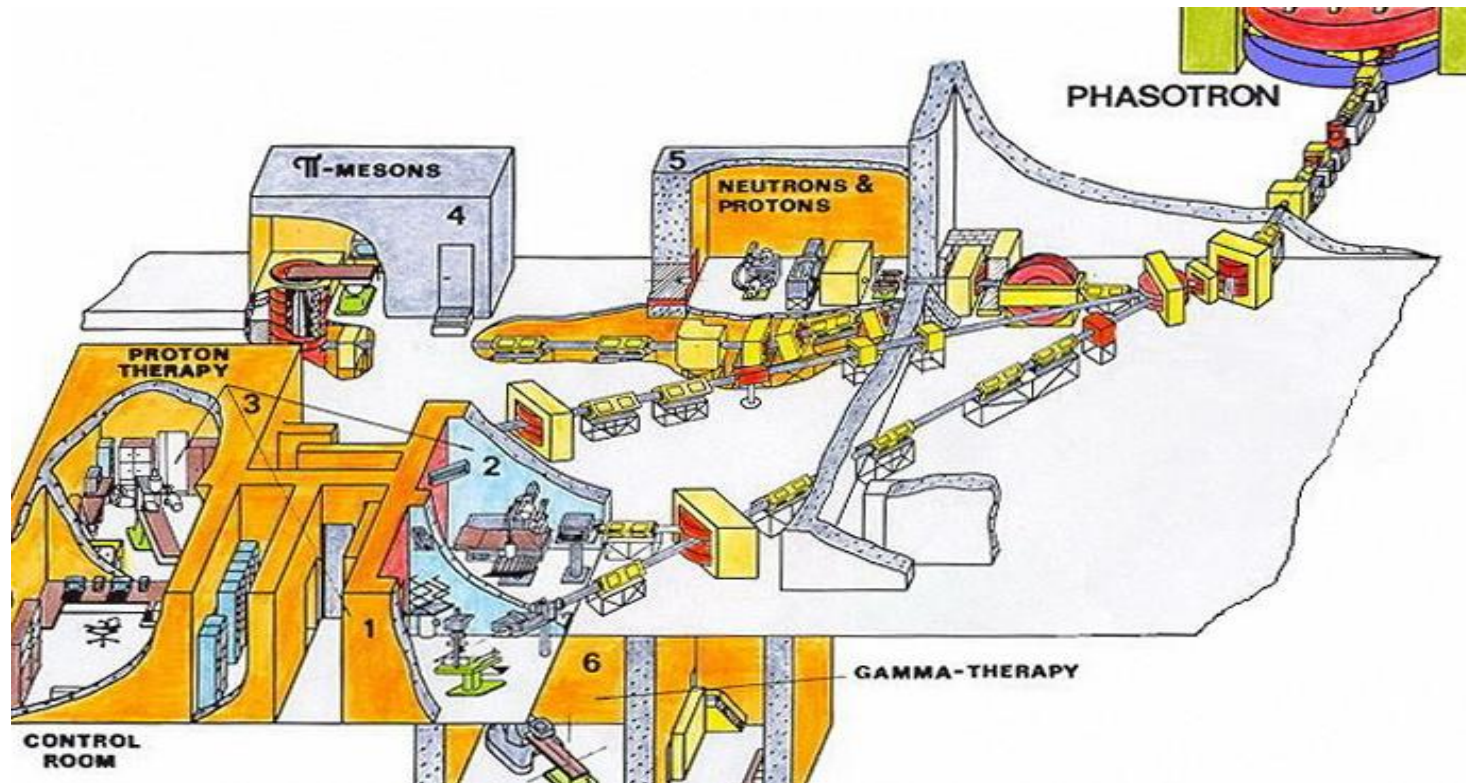
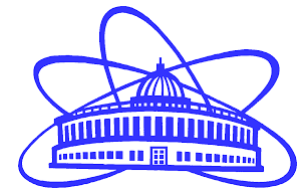
- JINR proton therapy since 1967
- 660 MeV proton beam of the phasotron
- Conformal treatment
- More than 1000 patients (~100 per year)
- Today: **Medico-Technical Complex (MTC)**
- **Various methods to treat oncological diseases:**



-- application of a proton beam of different energies for a wide range of neoplasms' locality (*box 1*),

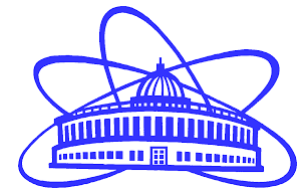
- the so-called “shoot-through” technique with a proton beam of maximum energy of 660 MeV (*box 3*),
- treatment of onco-gynecological patients (*box 2*),
- experiments to use such exotic particles in radiotherapy as negative pi-mesons (*box 4*),
- neutron therapy (*box 5*)
- and standard gamma therapy at the “Rokus” device (*box 6*).

JINR MEDICO-TECHNICAL COMPLEX

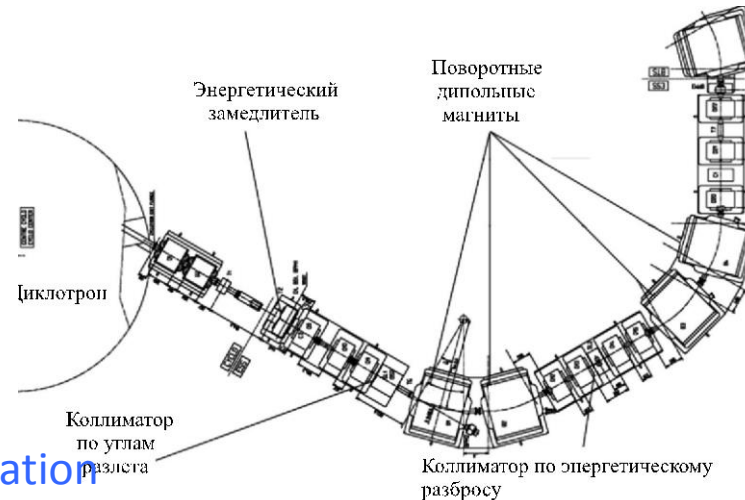
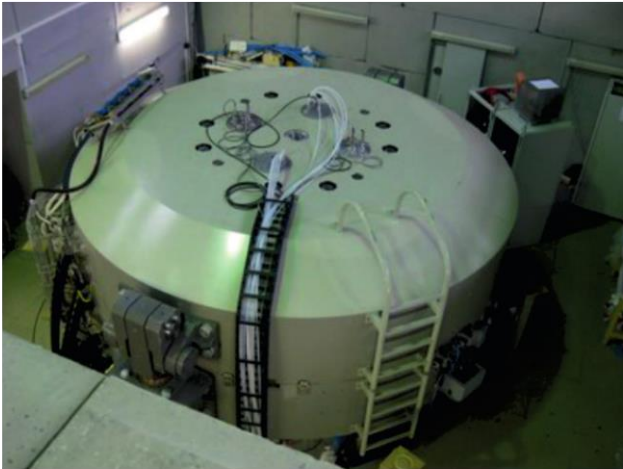


http://mtk.jinr.ru/index.php?Itemid=39&id=8&option=com_content&task=view&lang=english

Medical proton cyclotron IBA C235-V3 tests at JINR

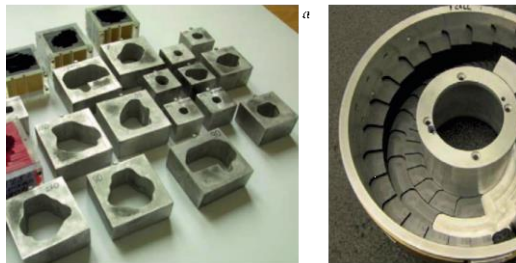


Cyclotron was delivered in Dimitrovgrad in September 2012



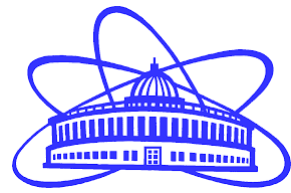
C235-V3 developed by JINR-IBA collaboration

Beam energy selection scheme [1]



Collimators and boluses manufactured by MTC at JINR (left) and the Bragg peak width regulator [1] used in double-scattering irradiation method

[1] S.V.Kostromin, E.M.Syresin, Trends in accelerator technology for hadron therapy, PEPAN Letters, 2013. 10, No. 7 (184), p.1346-1375//; С.А.Костромин, Е.М.Сырeсин, Тенденции в ускорительной технике для адронной терапии, Письма в ЭЧАЯ. 2013.т.10, № 7(184), с.1346-1375



JINR – IBA long-term COLLABORATION

Compact superconducting cyclotron for hadron therapy –C-400

- *///The construction of C400 was started in the framework of Archade project (France, Caen)///*
- JINR develops also a project of synchrotron applied for carbon ion therapy.
-

Proton centers

at research scientific institutions -- ITEP



4320 patients in the period 1969-2012 [1]

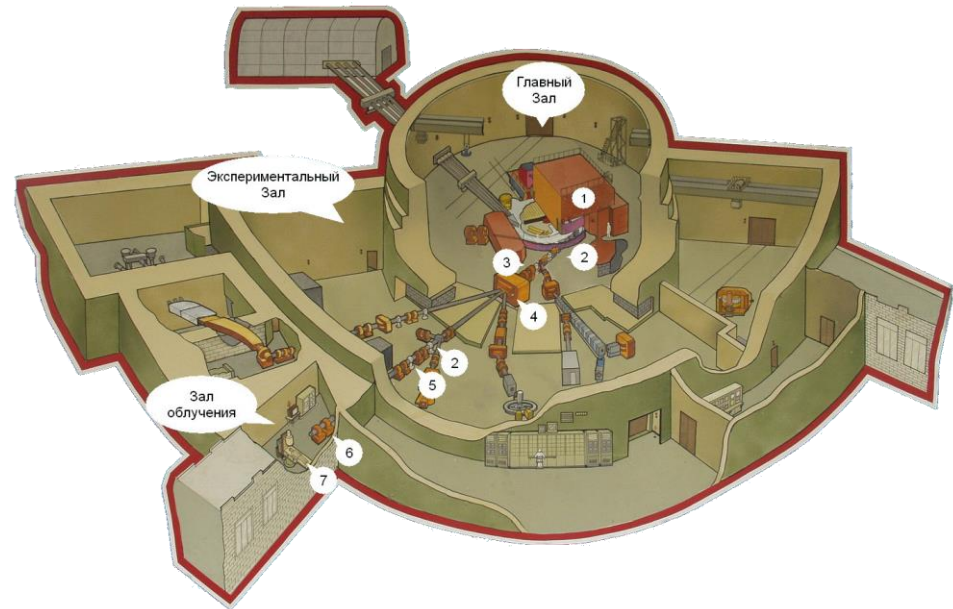
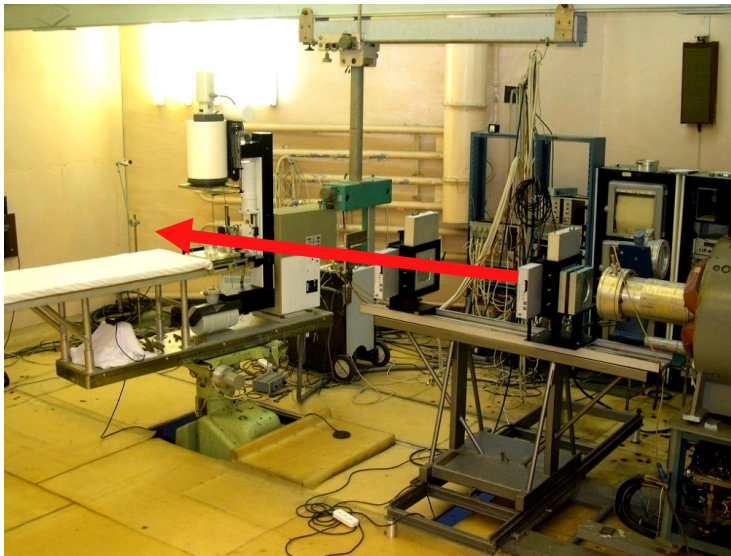
In 1968 ITEP followed JINR with the research program in radiation oncology at the 7.2 GeV proton synchrotron. Medical beam extraction up to 200 MeV with broad beams and ridge filter to create depth dose distribution, Since 1972 a Bragg plateau was used.

[1] Г.И.Кленов,
В.С.Хорошков, Адронная лучевая
терапия : история, статус,
перспективы, УФН, 186Б №8, 891-
911, Август 2016

Proton centers at research scientific institutions -- PNPI, Gatchina



– stereotaxic proton 1 GeV
proton beams,
In cooperation with CRIRR
Started in 1975, more than
1300 patients





Protons: 40 ÷ 80 MeV

Beam intensity: up to 100 μ A

1) Production of “generator isotopes”

Sr-82 (tau ~ 26 days) \rightarrow Ru-82 (tau~ 1 min)

2) ophthalmology

Proton centers at research scientific institutions -- INR



INR proton LINAC:

- Proton beam energy range: 70-220 MeV
- Mean intensity (can be varied) 0-100 μA ,
- Beam splitting to the low-intensity and high-intensity beams for simultaneous applications
 - in proton therapy and
 - in isotope production
- Puls length : 1 ms, Rep. rate 100 Hz,
- Production of Sr-82 for PET diagnostics
- The laser- based technology of production of Yb-168
- Investigations on neutron therapy and for the Gd neutron-capture therapy



Figure 1: The first proton therapy treatment room [1]

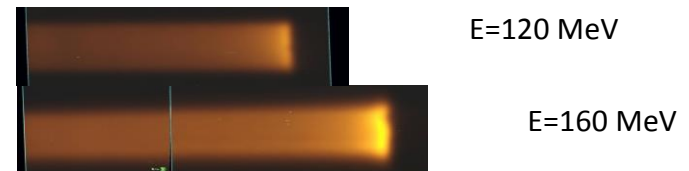


Figure 3: Medical proton beam visualization in the tissue equivalent plastic.

The beam diameter is always about 5 cm [1].

Proton medical centers under construction -- Dimitrovgrad

Medical center of proton therapy in Dimitrovgrad (Ulyanovsky region) --the first state center in Russian Federation, 1 200 pat-s/year



- **IBA C235-V3 cyclotron , cost covered by the federal budget in 2013**
- **Cost: from 14×10^9 rubles for Proteus-235, – grew up to 20×10^9 rubles at present (~ 300 mln euro), under investigation**
- **Plans: 2018**

Carbon ion beams (IHEP, Protvino)

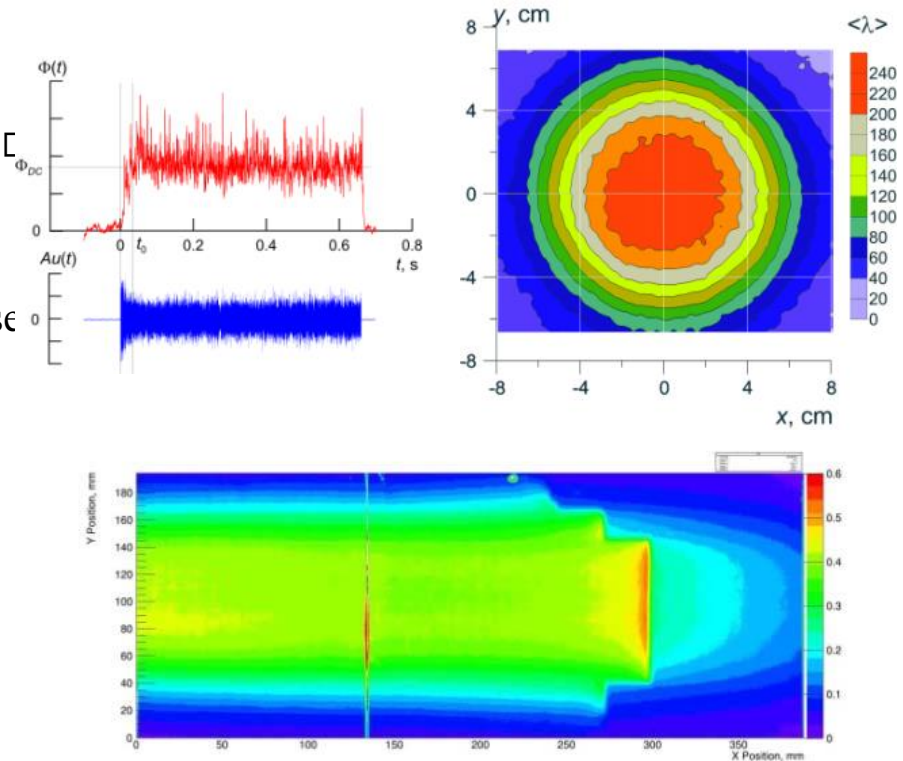


Accelerator Complex U70 of IHEP-Protvino

- Protons: 50–60 GeV, $1 \cdot 10^{13}$ protons per a 10 s cycle, or as a
- Light ions: 24–34 GeV per nucleon (kinetic), $5 \cdot 10^9$ bare ions per an 8 s cycle
- an ongoing upgrade program, see [1]

➤ **Plans for Center of proton-ion therapy at IHEP**

Figure 11 from [1]: Structure of carbon beam from the U70. Top left — temporal t-pattern (0.6 s long low-ripple spill via feedback-controlled slow stochastic extraction). Top right — spatial transverse (x, y)-pattern (flattened paraxial dose field with a diameter 6 cm of <5% non-uniformity via a PM rotating electromechanical wobbler). Bottom — spatial longitudinal s-pattern (30 cm of stopping range in a water phantom with the Bragg's peak visible).





Proton medical centers under construction

--Obninsk <http://www.protom.ru/>

Proton accelerator “Prometheus” in Obninsk

- On 23 November 2015 Employees of the Medical Radiological Research Center (Obninsk) launched clinical use of the medical proton complex "Prometheus" in Protvino, Russia, after the receipt of the state certificate by the JSC "PROTOM" authorizing the treatment of patients with head and neck, brain tumors.
- “Prometheus”
- In March 2017 a Russian proton accelerator "Prometheus" was installed in the Medical Radiological Research Center. A.F. Tsyba in Obninsk (Russia). The cost of Russian development amounted to 300 million rubles (about 40 mln euro).
- In 2018, treatment rooms for therapy should be put into operation.

“Prometheus” – New compact accelerator for proton therapy



<http://www.protom.ru/>



Some medical advantages:

- 1) larger irradiation dose to the tumor
- 2) Irradiation of multiple tumors
- 3) Optimized IMPT
- 4) Reduction of treatment duration
- 5) "Adaptive treatment" is possible
- 6) Irradiation of moving organs

- April 2015 года. Assembly of compact proton accelerator for Massachusetts General Hospital (Boston, USA). Photo: [protom.ru](http://www.protom.ru/)

<https://i1.wp.com/trv-science.ru/uploads/192-0066.jpg>

“Prometheus” (V.Balakin accelerator) :



<http://www.protom.us/our-facility>



- 2008 --installed in MIT (Boston), in 2014 – FDA received, 2015 – transferred to McLaren center,
- In 2015 another facility was brought to MGH(Boston).]
- March 17, 2017 -- registration certificate for medical device in Russia was received.

Parameters:

- energy – 70-330 MeV $\pm 0.15\%$
- **Intensity - 3×10^8**
- **Slow extraction 0.1 ÷ 10s**
- , “pencil beam” 5 mm,
- Diam 5m, Weight 15t, Power 50kW,
hall 7x9m²

Treatment room is ready. The movement of internal organs is two times lower than in lying position. So, vertical patient positioning is more preferable. No gantry.

http://www.protvino.ru/upload/medialibrary/672/protom_002.jpg

Ural Federal District of RF



Administrative center Yekaterinburg

Area^[1]

- **Total** 1,818,500 km² (702,100 sq mi)

Population (2010)

- **Total** 12,080,526

Nuclear Medicine cluster in the Southern Urals in the Russian Federation

Decision of the Public Council of the *State Corporation Rosatom* on June 24, 2016:
*Recognize the Ural Federal District as the basis for the development of nuclear
technology medicine*

Neutron therapy

Radionuclide therapy

Onco-ophthalmic applicators

Conformal DLT

Brachytherapy I-125

SPECT

PET centre

Cyber knife

Gamma Knife

- Strong school of Nuclear Medicine
- An excellent example of cooperation of medicine, physics, technology **and education !**
- Strong principles in work

**Federal program "Oncology" in the Southern Urals
Led by Acad.A.Vazhenin, The General Radiologist
of SU Federal District**

PLANS FOR PROTON THERAPY CENTER

Non-state, commercial, proton therapy medical center by MIBS

Dr. Berezin Medical Institute (MIBS) was founded in 2003.

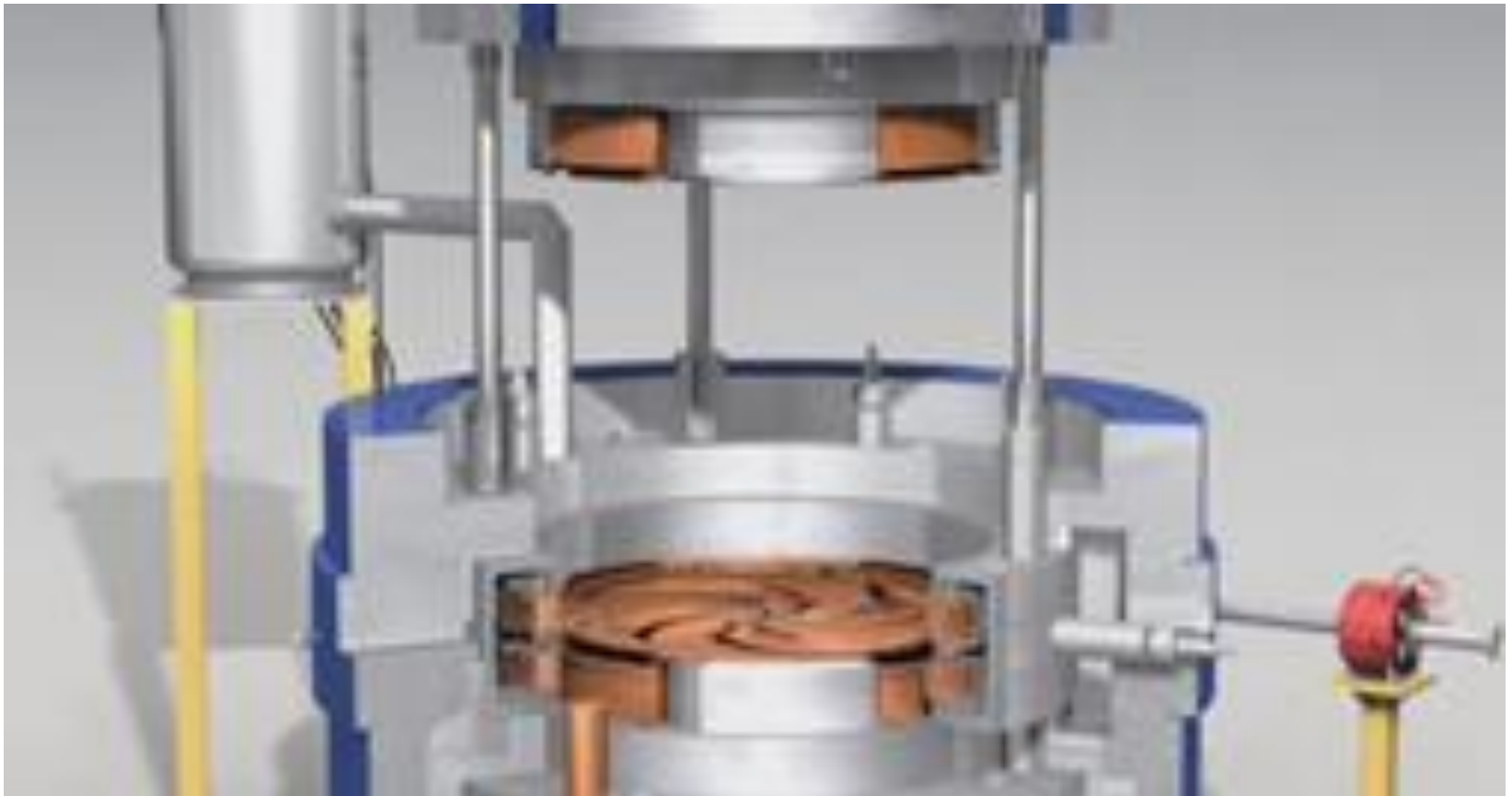
- Every fifth MRI examination in the country is carried out in one of MIBS' centres.
- MIBS is one of the pioneers in the Radiosurgery field in the Russian Federation. “Elekta’s Leksell Gamma Knife Perfexion ”, “Cyber Knife” and other modern equipment
- **June 2011 – Memorandum is signed between MIBS and the Governement of Saint-Petersburg on development of the Proton therapy center**

Investments: 150 mln \$

800 patients per year

Cyclotron ProBeam® (Varian)

Installed in Saint-Petersburg in 2016



Gantry at MIBS medical center



Treatment room



- 05.06.2017 – the 1st beam was obtained
- The official opening ceremony – in October 2018

[1] <https://riafan.ru/806129-v-centre-luchevoi-terapii-v-peterburge-poluchen-pervyi-puchok-protonov-iz-gentri>



Saint-Petersburg State University team

Laboratory of Ultra-High energy physics (in ALICE since 1992).

Laboratory of nuclear reactions

The expertise in the following fields:

1. Theoretical analysis (excitation function, different nuclear models) of the nuclear reactions

2. Target technologies, different target units,

3. Radiochemistry

4. Beam diagnostic

5. Detector development

6. GEANT and FLUKA simulations

7. Data analysis technique

➤ The main activity the Laboratory of nuclear reactions is connected with “Radionuclides production technology “

➤ Jointly for many years with the Department of Radiochemistry and the Laboratory of nuclear reactions and V.G. Khlopin Radium Institute.

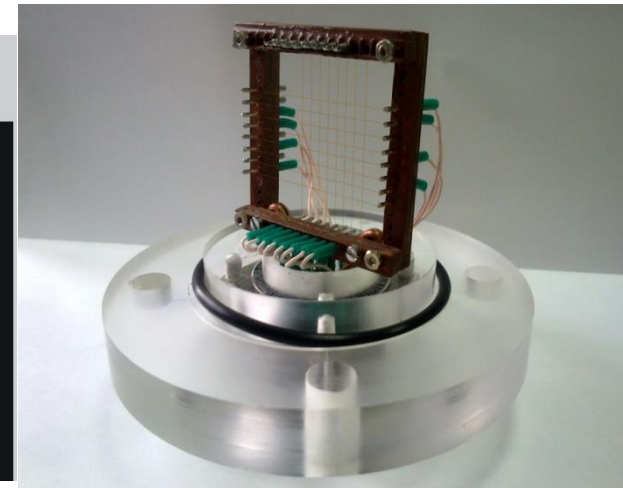
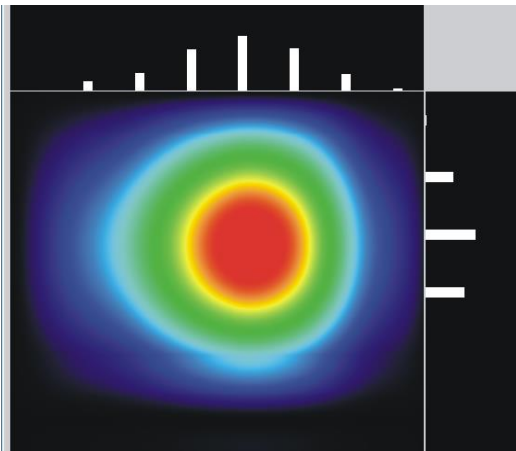
Laboratory of nuclear reactions:

Test of Si-detectors

Nuclear reactions

Nuclear medicine

Beam diagnostics





Models for Hadron therapy at SPbSU: Bragg Peak for protons in the non-uniform targets of complex geometry

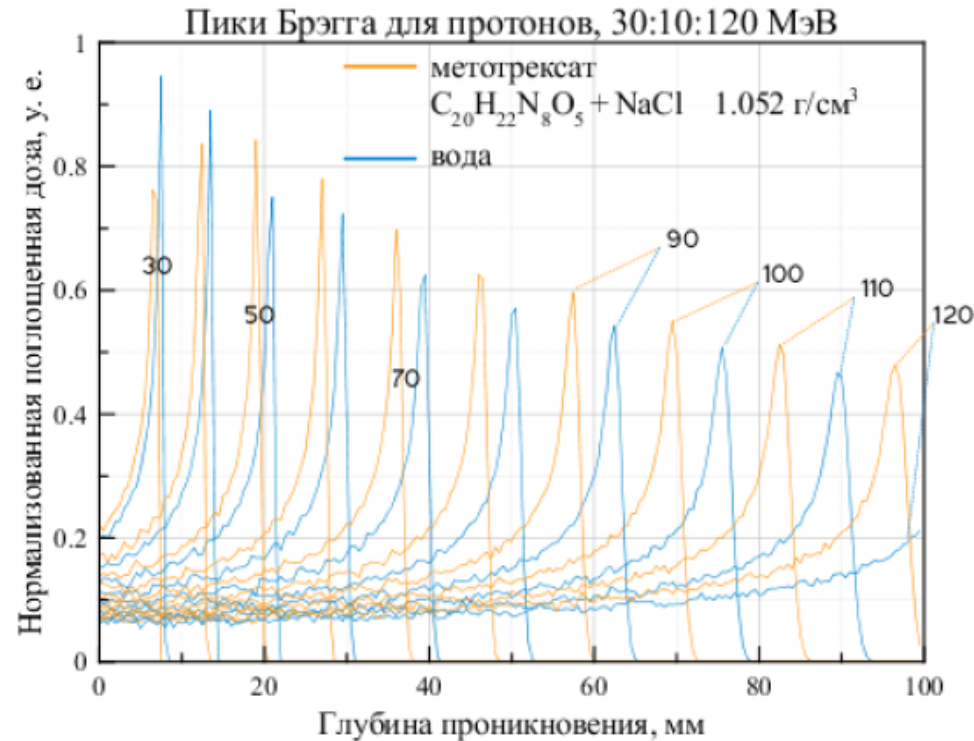


Рис. 23: Сравнение кривых Брэгга в воде и растворе метотрексата

**Bragg peaks for protons in non-uniform density tissues, Olga Ruban,
MS Dissertation, SPbSU, 2012**

Laboratory of nuclear reactions in nuclear medicine



Several directions of the R&D :

- 1) shaping the program of studies of selection of radioisotopes needed/requested/'desirable for therapeutic and diagnostic needs
- 2) analysis of ways of production of some selected radioisotopes using proton accelerators and nuclear reactors (a vast list of radionuclides may be discussed)
- 3) methods of extraction of these selected radioisotopes
- 4) new target units used for the radioisotopes production, R&D and practical demonstration of efficiency and performance production,
- 5) Metrology and standardization



Laboratory of nuclear reactions: Some plans for nuclear medicine.

- To continue radiosotopes production for theranostics (V.I.Zherebchevsky)
“Targeted therapy”, **Nuclear reactions for production of : ^{44}Sc , ^{117}Sb , ^{119}Sb ,**
[1]
- To study radiation effects on materials in isotopes production.
- In cooperation with Radium institute named after V.G.Hlopin and Institute of high molecular compounds
- Facilities: the proton and deuteron beams of MGC-20 cyclotron and neutron beams of the VVR-M reactor. New C-80 cyclotron at PNPI(Gatchina)

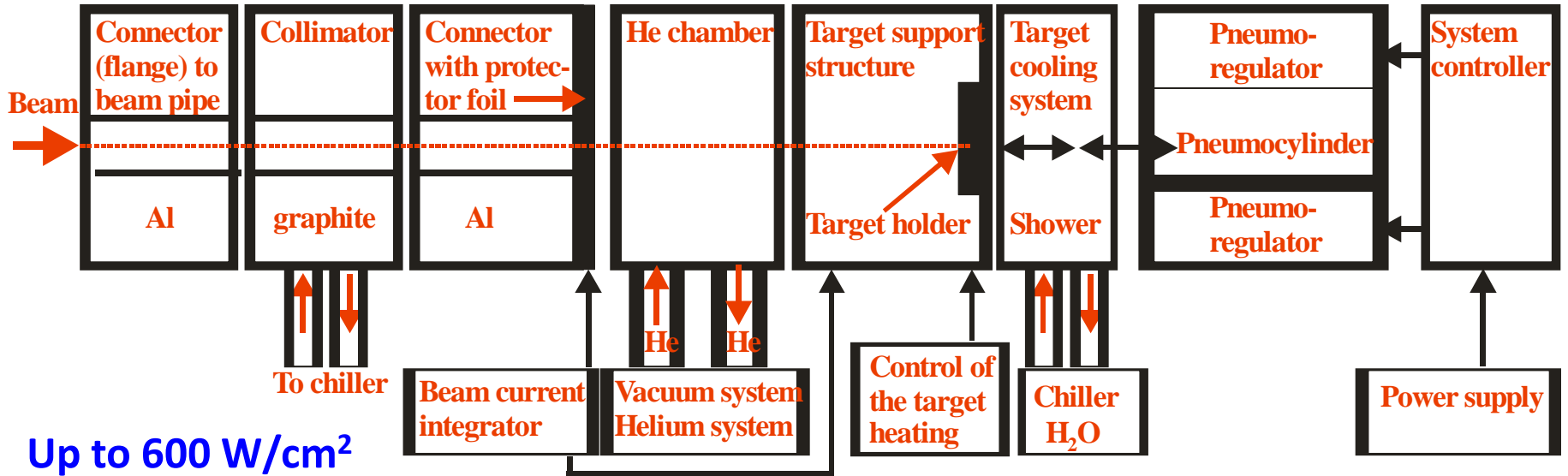
Various spectrometers might be applied (X-ray, gamma-, alpha, Mossbauer, conversion electrons and gamma-gamma correlations methods).

[1] “The study of the nuclear reactions for the production of antimony isotopes”,
V. I. Zherebchevsky, I. E. Alekseev, K. A. Gridnev, E. B. Krymov, T. V. Lazareva, N. A. Maltsev, R.
B. Panin, N. A. Prokofyev, S. Yu. Torilov, A. I. Shtamburg
Bulletin of the Russian Academy of Sciences: Physics. Volume 80, Issue 8, pp. 888–893, 2016.

Target system for high currents and high energy proton beams



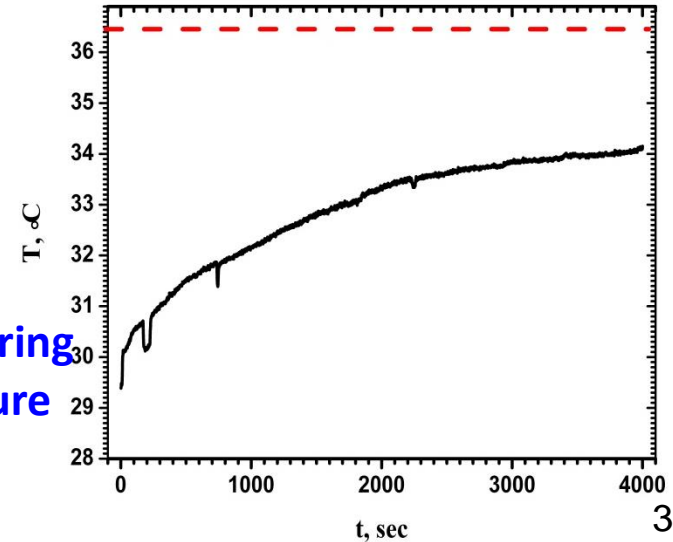
Target system



Up to 600 W/cm²



The on-line monitoring of target temperature



Laboratory of nuclear reactions:

Summer practice for school children

1. Oresident Phys.mat. Lyceum №30№ 239
2. Phys.mat. Lyceum №30
3. L.Fadeev Academy gimnazium



2017 г.

Conclusions

- High-Tech state-supported Hadron Therapy medical centers are needed in Russian Federation and in Saint-Petersburg
- Development and the fastest implementation of the most efficient methods of cancer diagnostic and therapy, including carbon ions, is a must for the North-West region of RF
- **One of the lessons learned – medical doctors should be involved in the leading positions of the hadron therapy project. But nobody knows how to do this.**
- The political aspects are VERY STRONG. The society should push politicians...
- The truly international efforts are needed: **The ENLIGHT++ partnership** is essential for efficient future developments.

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BACK-UP



Saint-Petersburg team “visiting card”:
the main activity since 1992 is for ALICE at the LHC,
however, not only...