Boris L. Zhuikov

History and Prospects of the Radioisotope Complex at the INR RAS

История и перспективы радиоизотопного комплекса в ИЯИ РАН

Международный семинар
«Развитие радиохимии и получение медицинских изотопов»
Институт ядерных исследований РАН, Троицк-Москва, 14 января 2022 г.

Main INR's Collaborators in Isotope Development and Production

- **Los Alamos National Laboratory, USA**
- **Brookhaven National Laboratory, USA**
- **Canada's National Facility TRIUMF, CANADA**
- **1st Milano University, ITALY**
- **GIP ARRONAX, FRANCE**
- **CURIUM (ZEVACOR Molecular), USA**
- **Institute for Physics and Power Engineering, Obninsk, RUSSIA**
- **Karpov Institute for Physical Chemistry, Obninsk**
- **Russian Research Centre of Roentgenology and Surgery Technologies, St-Petersburg**
- **Lomonosov Moscow State University**
- **Medical Radiological Research Cetre, Obninsk**
- **Production Association "Mayak", Ozersk**
- **Vernadsky Institute of Geochemistry and Analytical Chemistry, Moscow**
- **Institute of Physical Chemistry and Electrochemistry, Moscow**
- **Institute of Atomic Reactors, Dimitrovgrad**

Last International Projects on GIPP (Initiatives for Proliferation Prevention)

- **IPP - ISTC, 116 people, 6 Russian Institutions, LANL, BNL**

  "Co-Production of Palladium-103, Strontium-82, and Germanium-68 for Distribution and Medical Applications"
- **IPP – CRDF, 32 people, 4 Russian institutes, BNL**

  "Development of High-Specific activity and No-Carrier-Added Tin-117m for Radionuclide Therapy"

The main participants of creation radioisotope facility and isotope developments and production at INR RAS

Key staff at INR

V.M. Kokhanyuk

Yu.G. Gabrielyants

V.M. Chudakov

S.V. Ermolaev

Yu.V. Kisselev

INR management and accelerator leaders

V.A. Matveev

L.V. Kravchuk

A.V. Feschenko

V.L. Serov

Key Russian collaborators

N.A. Konyakhin (Cyclotron Co)

N.A. Kostenikov (Granov RRCRST)

S.V. Shatik (Granov RRCRST)

L.A. Tyutin (Granov RRCRST)

S.N. Kalmykov (MSU)

The most close and successful foreign collaborators

John Vincent (TRIUMF)

Dennis Phillips (LANL)

Eugene Peterson (LANL)

Suresh Srivastava (BNL)

Yves Thomas (ARRONAX)

Ferid Haddad (ARRONAX)

Jean-Francois Chatal (NAOGEN)

Maxim Kisselev (CURIUM PHARMA)

Milestones of Radioisotope Research and Development at INR RAS

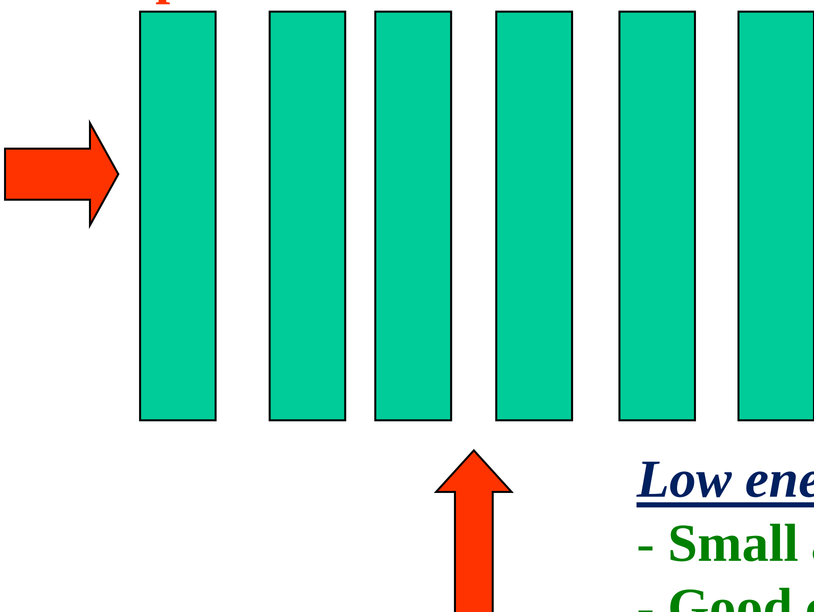
B.L.Zhuikov, S.V.Ermolaev. Phys.Usp., 2021, V. 64(12); Успехи физических наук, 2021, Т. 191, сс. 1387-1400

1989	**Organizing the Laboratory of Radioisotope Complex at INR**
1989	**Development of the complex for accelerating of radioactive heavy ions**
1989	**Starting of development ^{82}Sr-production at accelerators in Vancouver and Protvino and ^{82}Rb-genertaor developments**
1991	**Development and design of radioisotope target irradiation facility at INR-accelerator**
1992	**Construction of the radioisotope facility at INR-accelerator and the first target irradiations**
1993	**The first processing of the INR irradiated targets with ^{82}Sr at Obninsk and St. Petersburg**
1994	**Irradiation at INR and processing the targets with ^{109}Cd and ^{22}Na and supply to the customers**
1997	**Starting regular supply of Rb-targets with ^{82}Sr to LANL for certification and production**
2002	**Starting developments with ^{68}Ge and ^{103}Pd with LANL**
2003	**Starting of research developments with ^{117m}Sn with BNL**
2006	**Starting of research and developments for ^{225}Ac from Th-targets**
2007	**Design and approval of hot cell facility at INR**
2014	**Completion clinical trials and certification of Russian ^{82}Rb-generator at St. Petersburg**
2015	**Starting developments of new ^{213}Bi-generator**

Advantages and disadvantages of targetry at different proton energy

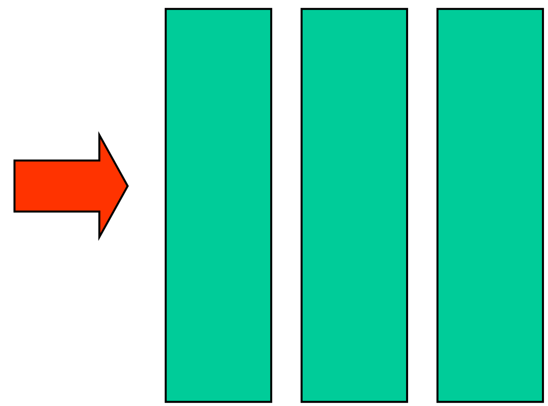
High energy 500-800 MeV (p, xp yn)

- **Low dE/dx (low energy release)**
- **Wide water gaps (easy cooling)**
- **Low cross-sections**
- **Large amount of impurities**
- **Expensive beam**



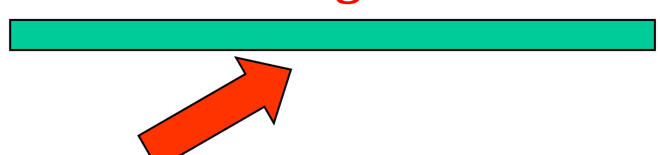
Middle energy 70-200 MeV (p, xp yn)

- **High dE/dx (high energy release)**
- **Narrow water gaps (difficult cooling)**
- **High cross-sections**
- **Small amount of impurities**



Low energy 15-40 MeV (p, 1-3n)

- **Small amount of impurities**
- **Good cooling**
- **Restricted spectrum of isotopes**
- **Enriched target material**



BEAM DIRECTIONS

Accelerator Facilities with High Intensity Proton Beam of Intermediate Energy

Los Alamos National Laboratory (NM, USA), 100 MeV, 250 μA

Brookhaven National Laboratory (NY, USA), 200 MeV, 160 μA

TRIUMF (Vancouver, Canada), 110 MeV, 500 MeV, 80 μA

Institute for Nuclear Research (Troitsk, Russia), 160 MeV, 120 μA

iThemba Laboratory (Cape Town, South Africa), 66 MeV, 250 μA

ARRONAX GIP (Nantes, France), 70 MeV, 2 x 150 μA

ZEVACOR (Indianapolis, USA), 70 MeV, 2 x 250 μA

Proposed Accelerator Facilities for Radioisotope Production at High Intensity Proton Beam of Intermediate Energy

- **Proton Engineering Frontier Project, KOMAC (Gyoungju, South Korea)**
  LINAC - 100 MeV, >300 μA
- **Legnaro National Laboratory, INFN (Padova, Italy)**
  Cyclotron - 70 MeV, 2x400 μA
- **Arizona Isotopes Science Research Corp. (USA)**
  Cyclotron - 70 MeV, 2x350 μA
- **South African Isotope Facility (South Africa)**
  Cyclotron – 40-70 MeV, 150 μA
- **Institute of High Energy Physics of Kurchatov National Center (St. Petersburg, Russia)**
  H^- Cyclotron – 70 MeV: production of ^{82}Sr
- **Institute for Nuclear Research of National Academy of Sciences of Ukraine (Kiev)**
  H+ Cyclotron, 70 MeV, 100 μA (^{82}Sr production from RbCl-target)

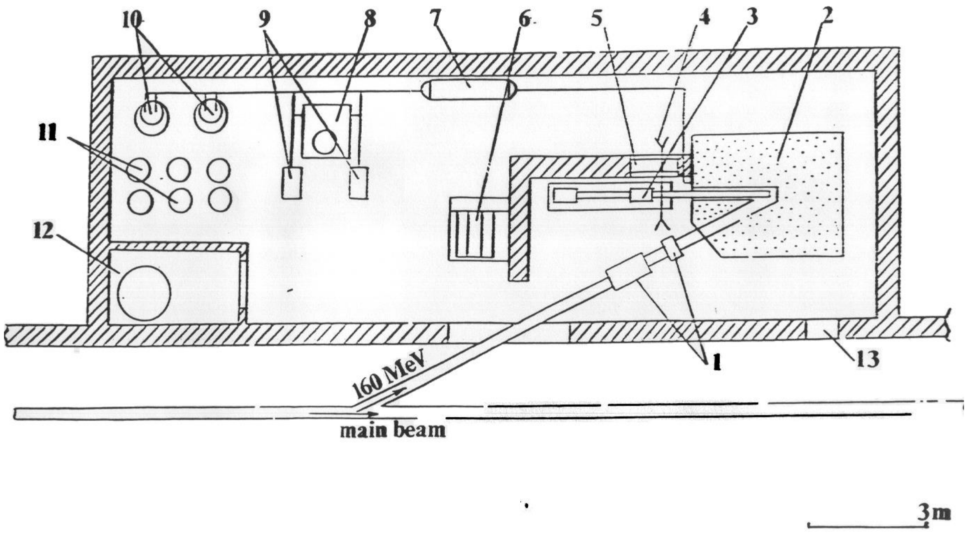
- **Institute for Nuclear Research (Troitsk, Russia)**
  H^- Cyclotron – 70 (120) MeV, 750-1000 μA: production of ^{82}Sr, ^{117m}Sn (^{225}Ac, ^{223}Ra)

Destruction of the first metallic Rb-target under water

(TRIUMF in Vancouver, together with John Vincent, 1988)

Target Irradiation Facility for Isotope Production at Linear Accelerator of Institute for Nuclear Research, Troitsk

(under operation since 1992)



Proton energy: 158 MeV

***(options:* 143,127,113,100,94 MeV)**

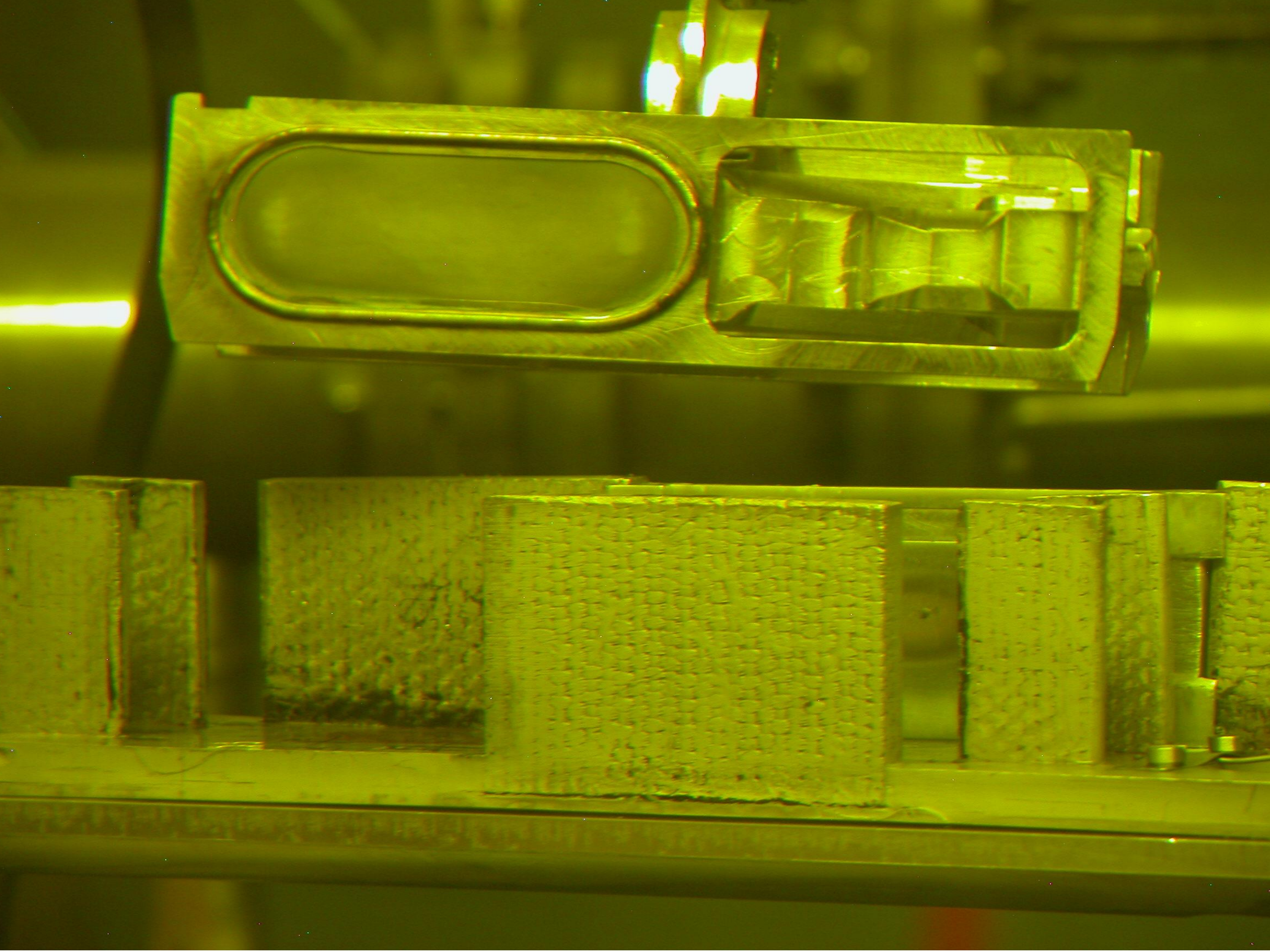
Typical beam current: 120 μA

PRODUCED RADIONUCLIDES:

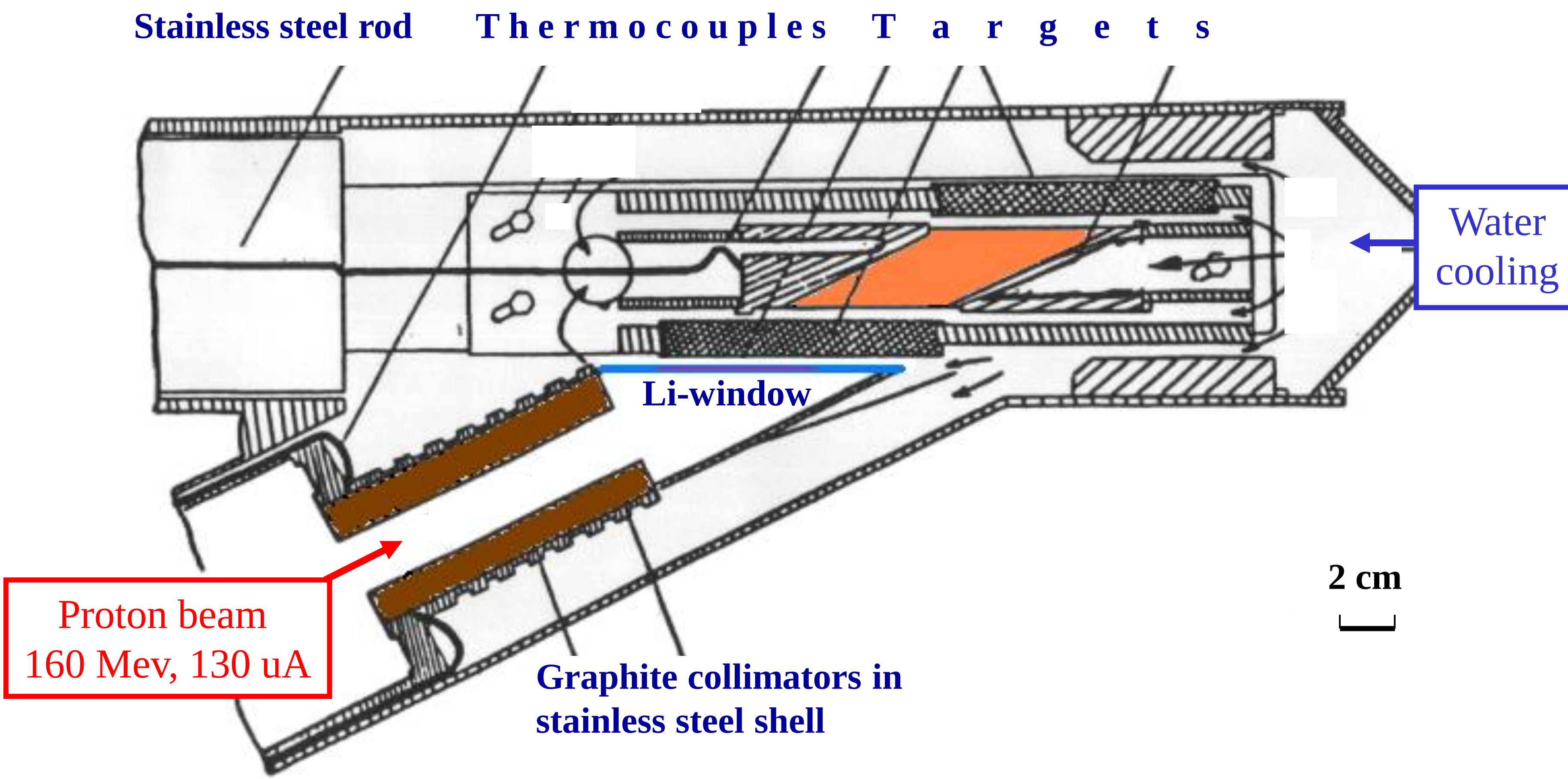
^{82}Sr, ^{225}Ac, ^{68}Ge, ^{117m}Sn, ^{103}Pd

Under development:

^{72}Se, ^{230}Pa, ^{223}Ra, ^{64,67}Cu



Target holder with graphite collimators and lithium beam window at INR facility

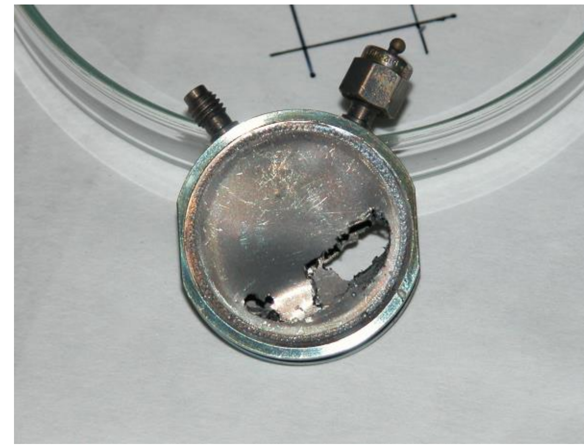


What happens if the target requirements are not fulfilled?
(not only thermal, but also radiation and chemical impact)

Aluminum

Graphite

Molybdenum



Antimony in stainless steel

Isotopes Produced in INR and Possible Activity Generated in One Accelerator Run at 120 μA

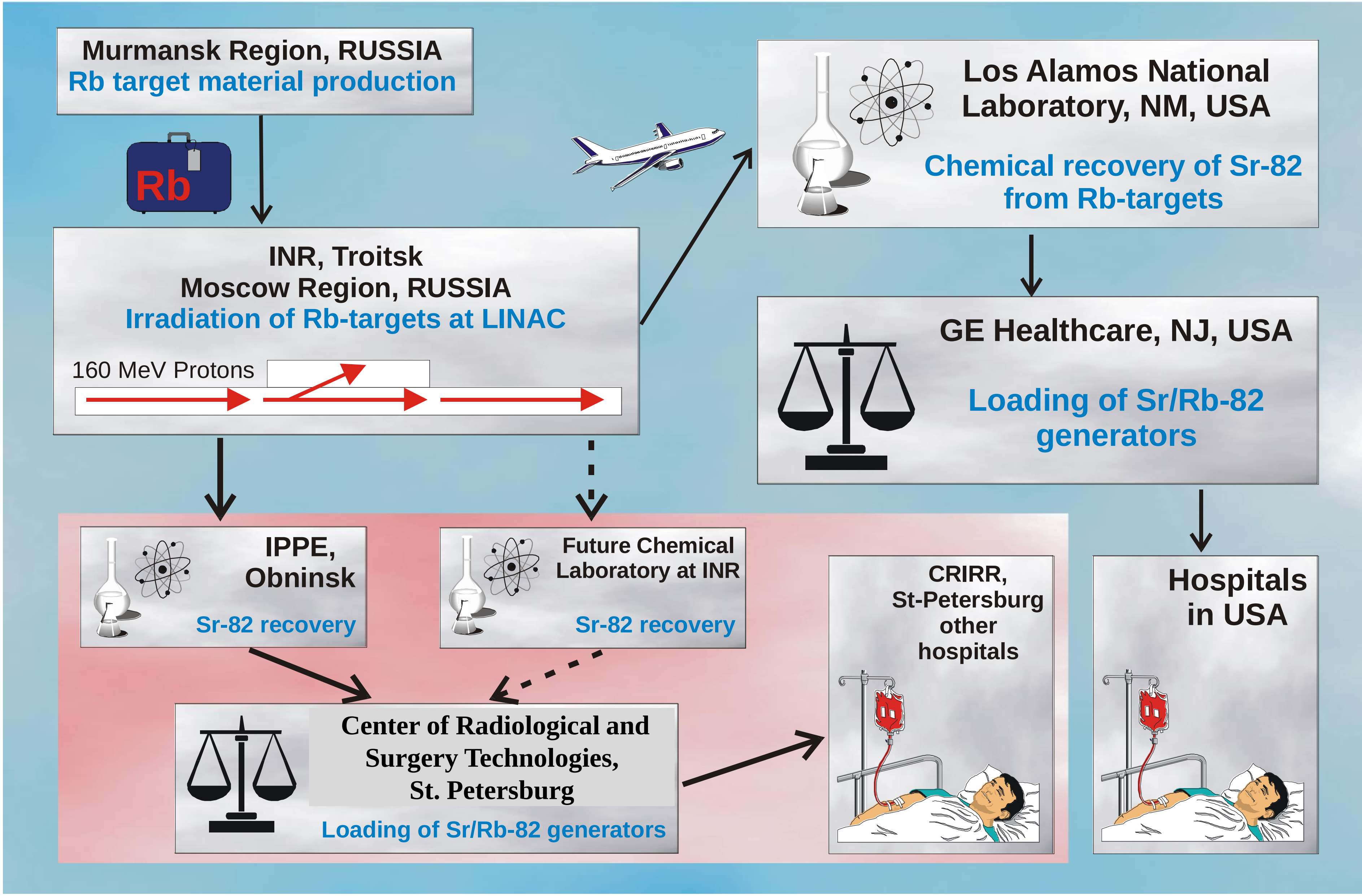
Radio-nuclide	Half life period	Target	Energy range, *MeV*	Bombardment run period, *hr*	Activity produced in one run at EOB, *Ci*
Sr-82	25.5 d	Rb	100-40	250	11
Na-22	2.6 y	Mg, Al	150-35	250	2
Cd-109	453 d	In	150-80	250	2
Pd-103	17 d	Ag	150-50	250	50
Ge-68	288 d	Ga, GaNi	50-15	250	0.5
Sn-117m	14 d	Sb, TiSb	150-40	250	3
Ac-225	10 d	Th	150-40	250	6
Ra-223	11.4 d	Th	150-40	250	12
U-230	20.8 d	Th	100-15	250	0.5
Se-72	8.5 d	GaAs	60-45	250	3
Cu-67	62 hr	Zn-68	150-70	100	10
Cu-64	12.7 hr	Zn	150-40	15	15
Ti-44	47 yr	Sc	60-20	250	0.01

Green – regular mass production

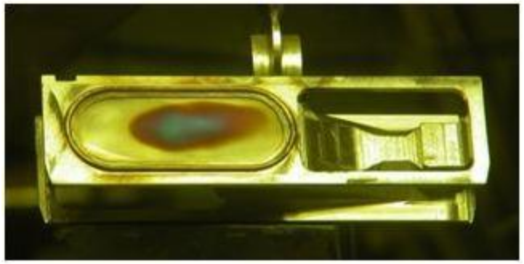
Blue – technology developed, test samples supplied to customers

Red – production method developed, technology under development

Production and Transportation Scheme of Strontium-82



Processing of INR metallic rubidium target for recovery strontium-82 at Los Alamos



150 Rb-targets irradiated at INR were processed at LANL, plus 22 at Russian facilities

About 350,000 US patients passed diagnostics with isotopes produced at INR, and more than 2,000,000 patients – with isotopes produced with mutually developed methods

Virtual Isotope Center- supplementing and extending existing availability of medical isotopes (organized by US DOE)

Одиннадцатое заседание
Комиссии по модернизации и технологическому развитию экономики России
(Обнинск, 29 апреля 2010 года)

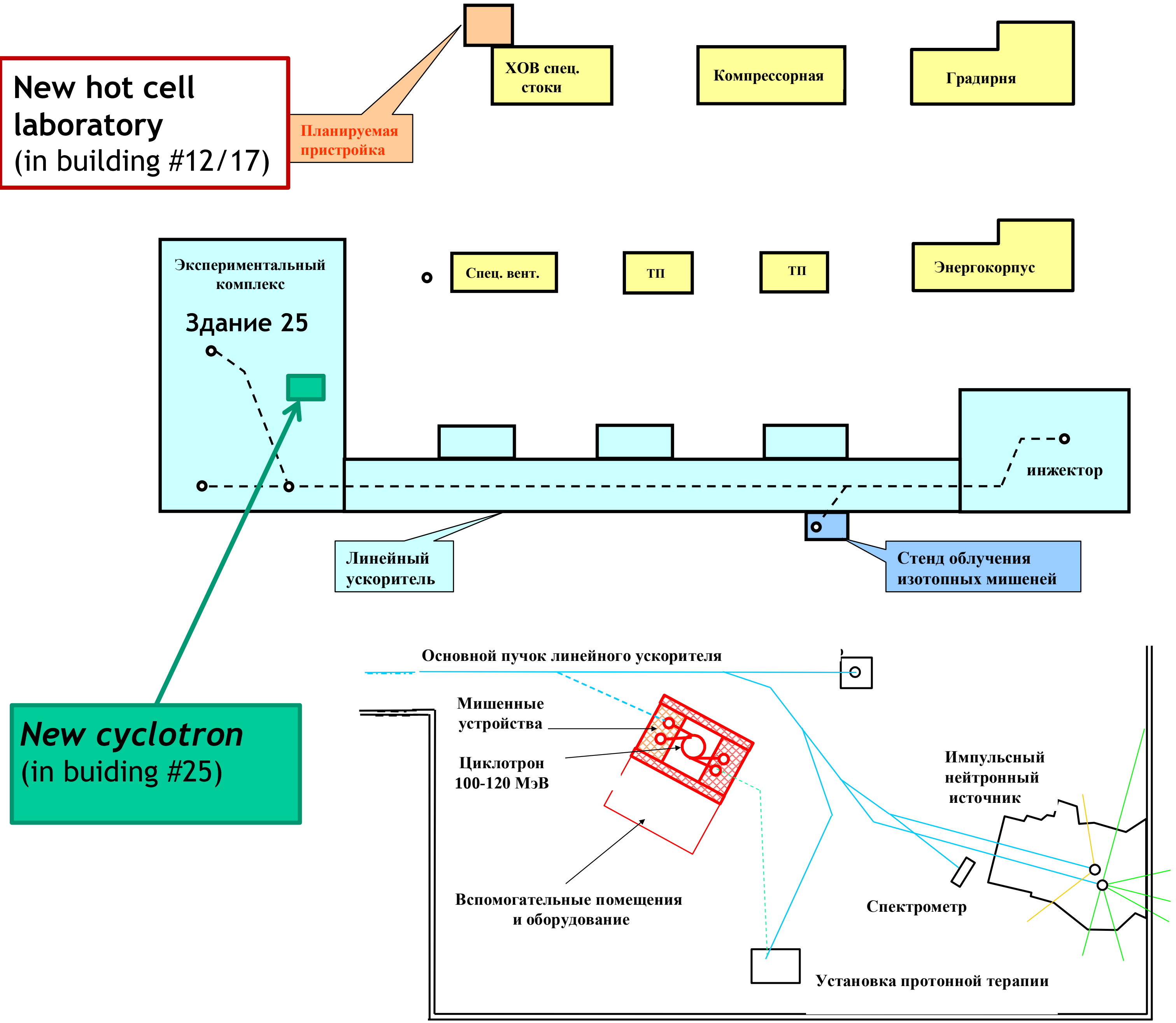
Дмитрий Анатольевич Медведев (Dmitriy Medvedev) – Президент России:

"По ядерным медицинским технологиям – вещь очевидная, они нашей стране очень нужны… Наша задача – научиться применять здесь наиболее передовые технологии; одним из наиболее перспективных методов, которые сегодня доказали свою эффективность, являются радионуклидные методы, радионуклидная диагностика и терапия…. У нас существует солидная научно-техническая база для производства радиофармпрепаратов, есть и позитивный опыт применения самых передовых технологий диагностики и лечения. К сожалению, это в основном импортные технологии."

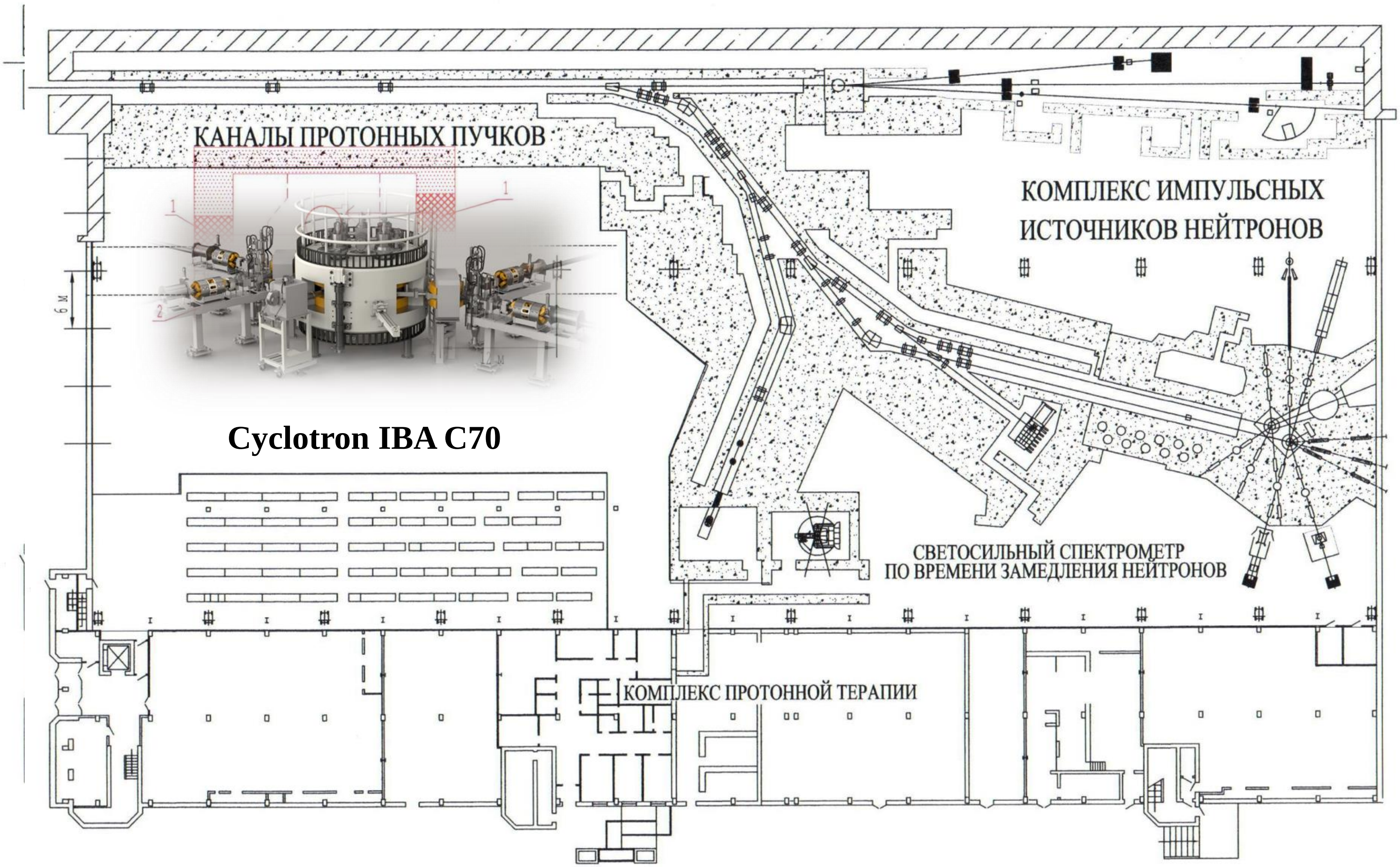
Татьяна Алексеевна Голикова — Министер здравоохранения и социального развития России:

"…**Генератор стронций/рубидий-82** применяется при диагностике пациентов с подозрением на заболевание коронарной артерии. Кроме этого, он может применяться при изучении функций головного мозга, желудочно-кишечного тракта, печени и почек. В настоящее время генератор рубидий-82 не производится ни в Европе, ни в Азии. **Он является отечественной разработкой Института ядерных исследований РАН.** Плановый выпуск генераторов – до 500 штук в год в расчёте до 2015 года. Из них для покрытия потребностей России нужно 300 штук, соответственно, остальные 200 могут быть направлены на экспорт."

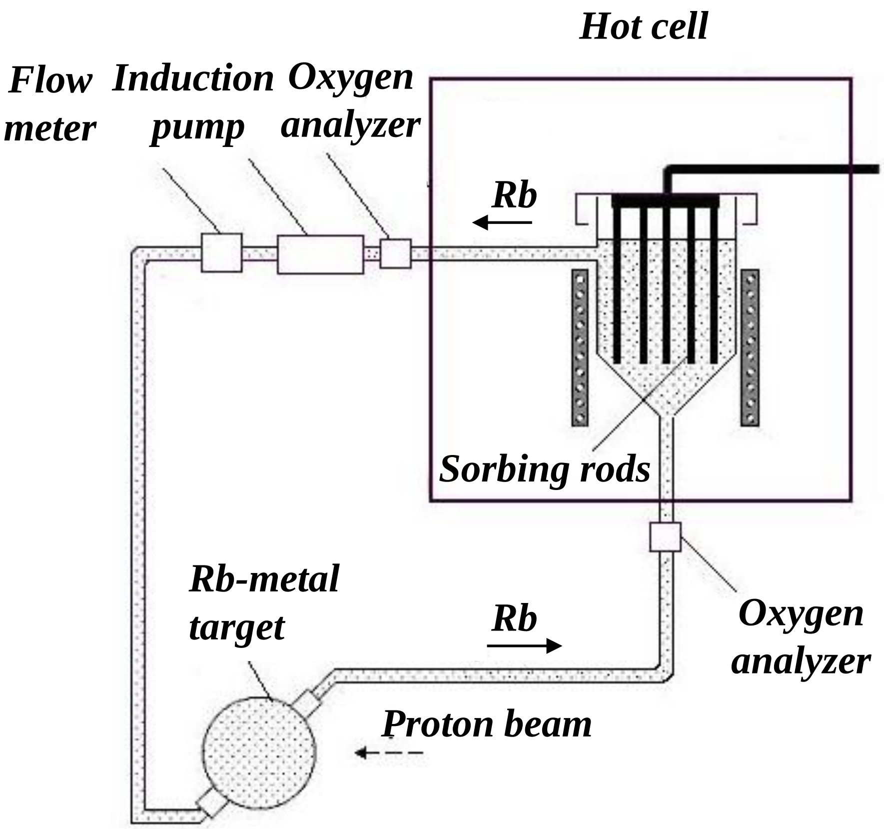
Existing and new future installations for isotope production at INR

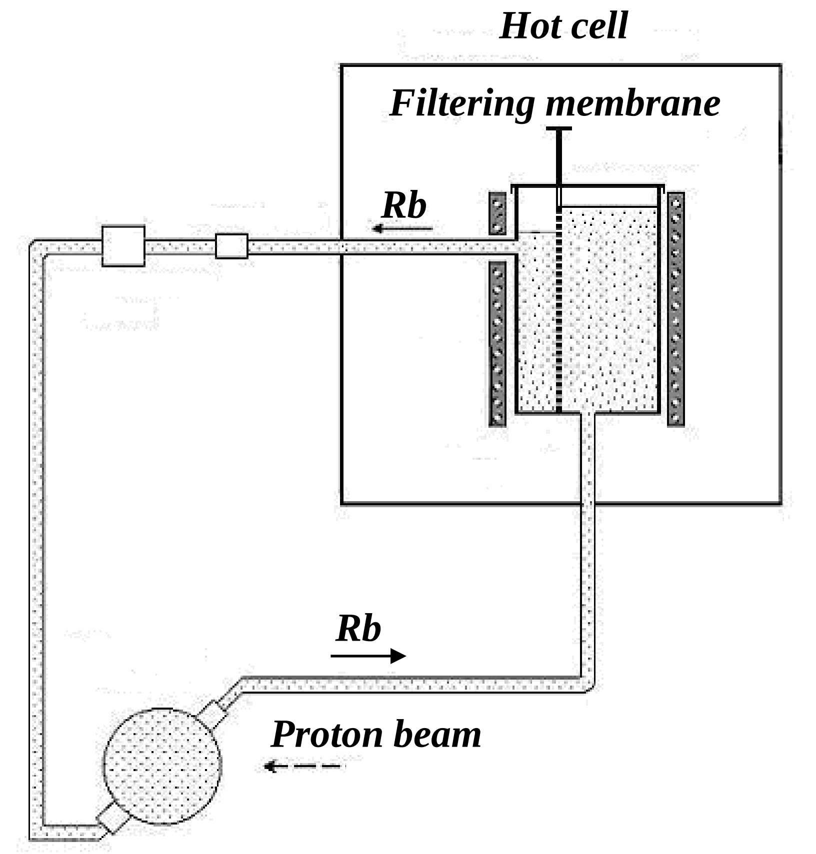


Proposed construction of IBA cyclotron in the Existing Building #25 at INR RAS
(H^- 70 MэB)



Future Development of On-Line ^{82}Sr-Production

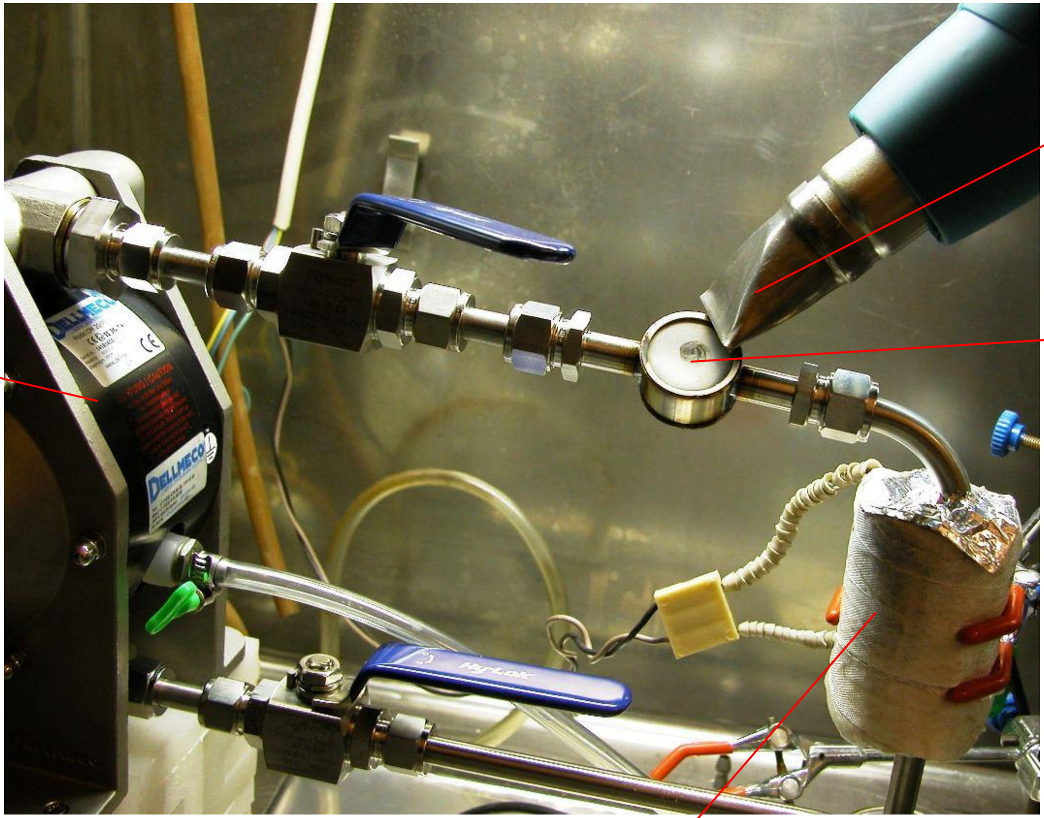




Target material	Rb+3%O (T_m=10°C)
Rb volume	1.5 L
Rb flow	5-10 L/min
Target diameter	8 cm
Energy release:	13 kW

Beam current	500 μA
Proton energy range	63-36 MeV
Production yield:	0.4 mCi/μA.hr
Production capacity ^{82}Sr	4.5 Ci/day at EOB
	2.5 Ci/day at consumption
	500 Ci/year at consumption

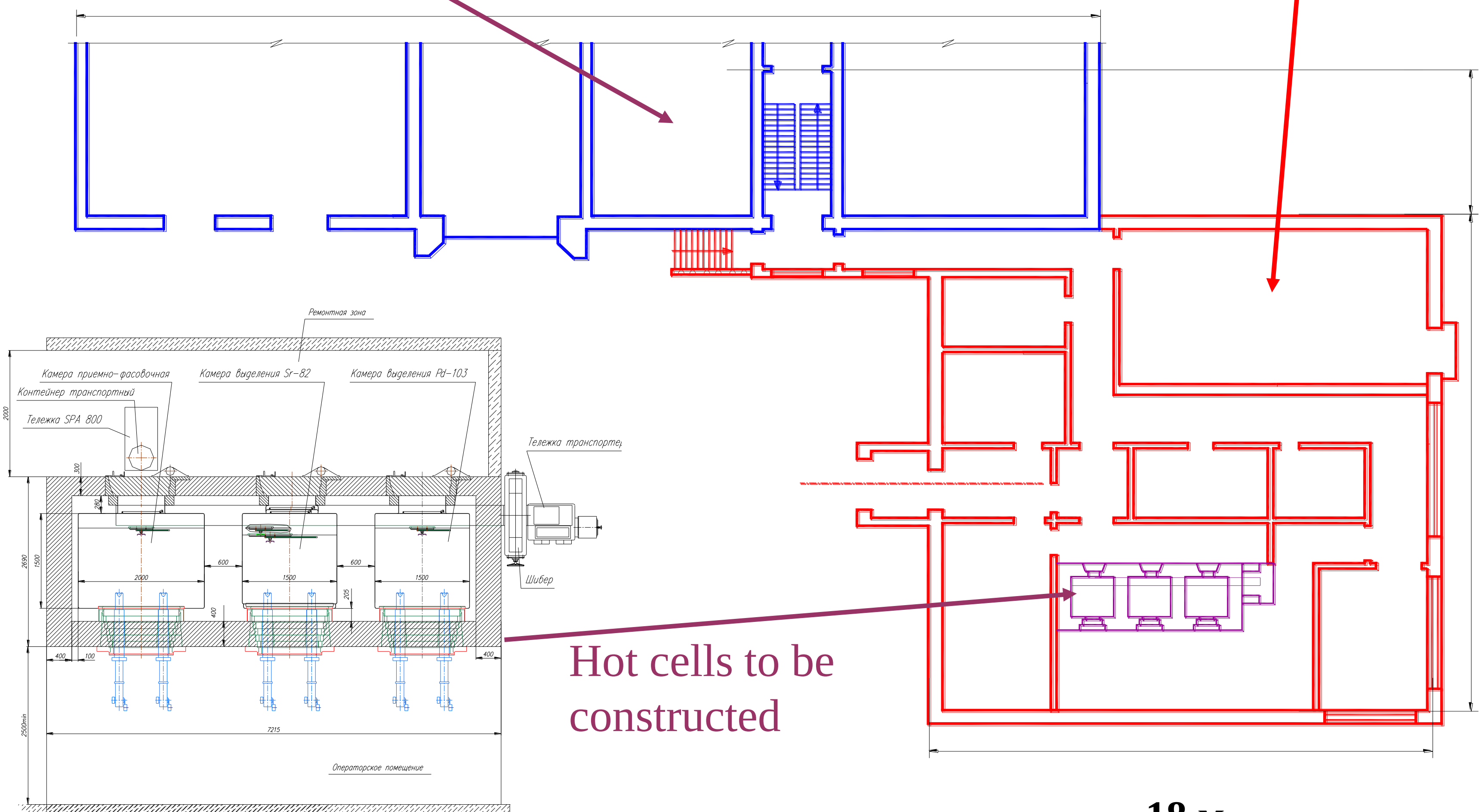
Experimental Setup for Investigation of Sr-Sorption from the Loop of Metallic Rubidium



Future hot cell laboratory at INR RAS in Troitsk

Proposed GMP-laboratory for generator loading in the existing building#17 at INR RAS

New building #12/17 with hot cells to be constructed



Possibility of Medical Isotope Production at INR

RADIO-NUCLIDE	APPLICATION	HALF-LIFE	ANNUAL PRODUCTION, *Ci*		PATIENT AMOUNT (per year)
			Linear accelerator	New cyclotron 70 (120) MeV	
^{82}Sr	PET- diagnostics (cardiology)	25 d	30	500	1 000 000
^{117m}Sn	Therapy, γ-diagnostics (bone cancer, cardio vascular disease)	14 d	10	30	1 000
^{67}Cu	Therapy (oncology)	62 h	20	100	1 000
^{64}Cu	Therapy, PET- diagnostics (oncology)	12.7 h	150	700	1 000
^{72}Se	PET- diagnostics (oncology)	8.5 d	15	60	80 000
^{103}Pd	Therapy (cancer of prostate, liver, mammary gland, rheumatoid arthritis)	17 d	200	800	10 000
^{225}Ac	Therapy (oncology)	10 d	8	(100)	(100 000)
^{223}Ra	Therapy (bone cancer)	11.4 d	20	(500)	(300 000)

Problems to be solved in R&D for medical isotope production in Russia

1. To overcome agency barriers in the disposition of funds for R&D

2. To organize an effective international collaboration with highly developed countries

3. To provide sufficient governmental funding to establish new facilities or upgrade the existing facilities

4. To form a qualified and independent international committee for distribution of funds to create and realize isotope projects

5. To reduce bureaucratic regulations (without prejudice to safety and security)

6. To prepare highly-qualified specialists