Applied research at NICA facility: new gates for cooperation in life sciences, materials sciences, and nuclear technology

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(on behalf of the ARIADNA collaborations)

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Joint Institute for Nuclear Research

India-JINR Workshop on Elementary Particle and Nuclear Physics, and Condensed Matter Research
16-19 October 2023

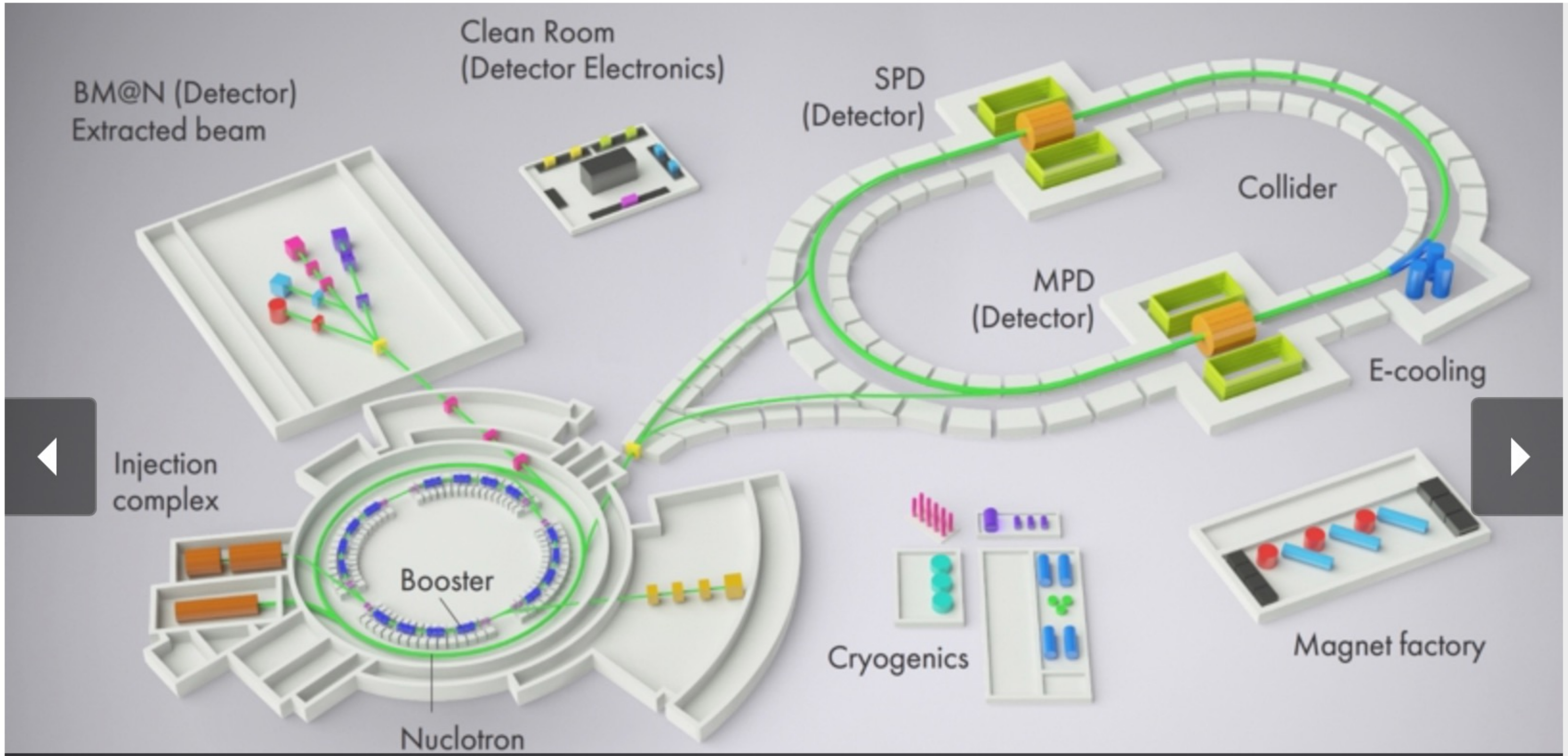
NICA MEGA-SCIENCE PROJECT

Nuclotron-based
Ion Collider fAcility

ENG | RUS

Search

- NICA Physics
- NICA Complex
- Megaproject
- Education
- Innovation
- Media & Events
- Contacts
- Review Committee



NICA Scheme
Superconducting accelerator complex NICA

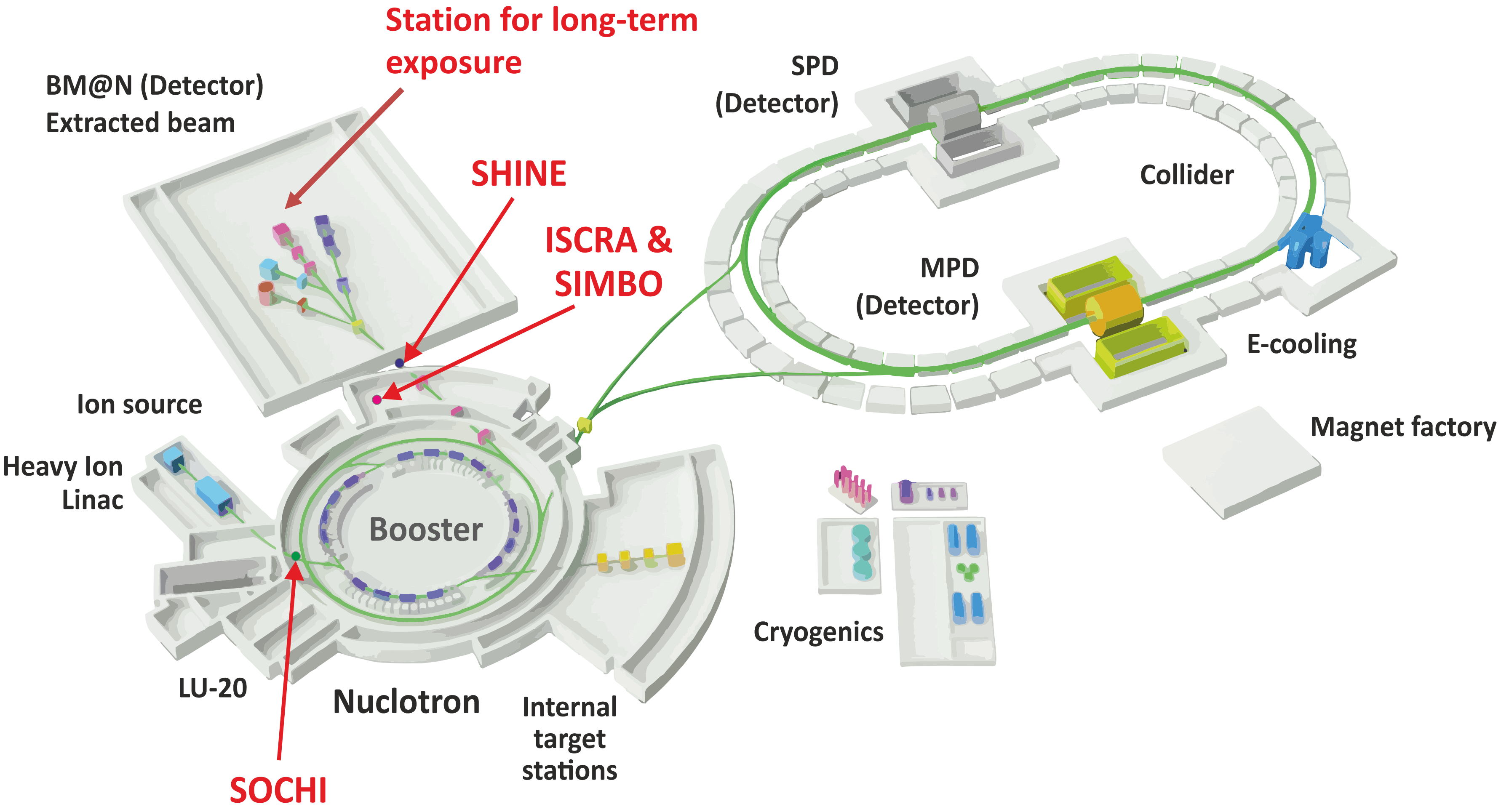
NICA (**N**uclotron-based **I**on **C**ollider f**A**cility) is a new accelerator complex designed at the Joint Institute for Nuclear Research (Dubna, Russia) to study properties of dense baryonic matter.

After puting the NICA collider into operation JINR scientists will be able to create in the Laboratory a special state of matter in which our Universe stayed shortly after the Big Bang – the Quark-Gluon Plasma (QGP).

Start of the construction: 2013.
Commissioning: 2022.

Applied Research and Innovations @ NICA

The Applied Research Infrastructure for Advanced Developments at NICA fAcility (ARIADNA)



APPLIED RESEARCH @ NICA

ARIADNA beamlines

The Applied Research Infrastructure for Advanced Developments at NICA fAcility (ARIADNA) will include:

(1) Beamlines with magnetic optics, power supplies, beam diagnostics systems, cooling systems, etc.

(2) Experimental zones equipped with target stations for users (detectors, sample holders, irradiation control and monitoring system, etc.)

(3) Supporting user infrastructure (areas for deployment of user's equipment, for sample preparation and post-irradiation express analyses, etc.)

Low-energy ion beams available at HILAC 3.2 MeV/nucleon	Intermediate-energy ion beams available at Nuclotron 150-1000 MeV/nucleon	High-energy ion beams available at Nuclotron up to 4.5 GeV/nucleon
Life sciences, Radiation damage to microelectronics, Materials science, Novel relativistic nuclear technology		

Protons and ions with *Z* = 2 to 92

Irradiation of decapsulated microcircuits and solid materials with 3.2 MeV/nucleon ions.

Ions: $^{12}C^{6+}$, $^{40}Ar^{18+}$, $^{56}Fe^{26+}$, $^{84}Kr^{36+}$, $^{131}Xe^{54+}$, $^{197}Au^{79}$

Irradiation of capsulated microcircuits with 150-350 MeV/nucleon ions. Ions like $^{197}Au^{79+}$ are decelerated in the capsule to 5-10 MeV/nucleon.

500-1000 MeV/nucleon ions be available at the target station for biological sample irradiation.

Ions: $^{1}H^{1+}$, $^{2}D^{1+}$, $^{12}C^{6+}$, $^{40}Ar^{18+}$, $^{7}Li^{3+}$

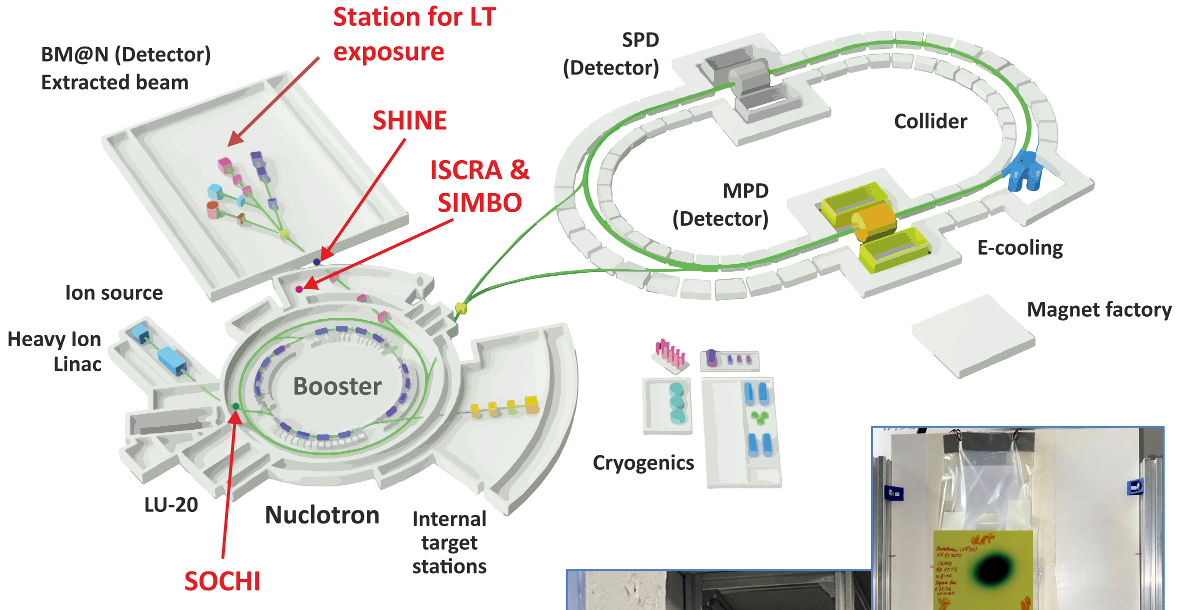
Target station will be equipped with targets from C to Pb and with the systems of beam and target diagnostics, positioning, thermometry, synchronization, radiation control, and data acquisition.

ARIADNA RESEARCH INFRASTRUCTURE: CURRENT STATE AND RECENT DEVELOPMENTS

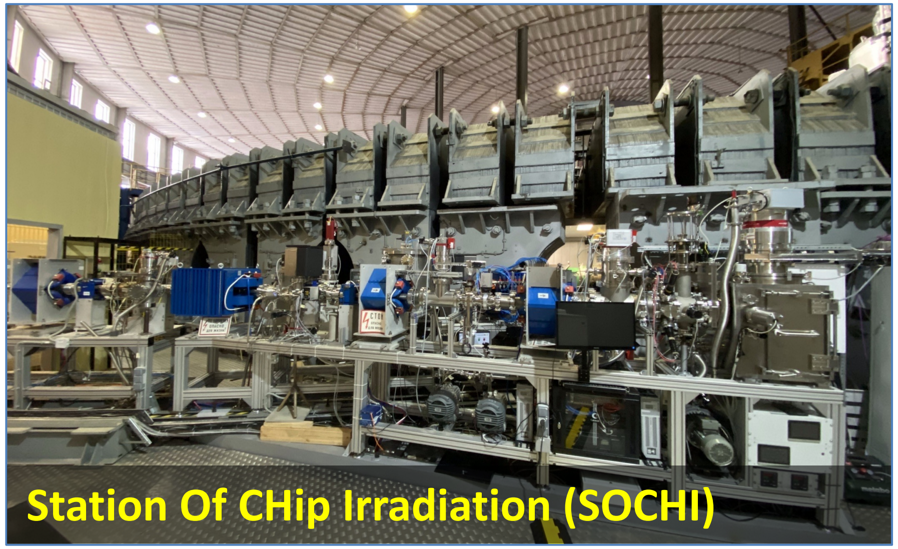
The progress was recently made in development of the NICA target stations for applied research.

In December 2021, the beamline and **Station Of CHip Irradiation (SOCHI)** was completed.

In December 2022, the **prototype of the Target station for long-term exposure with high energy ions** was assembled at the outgoing beam available behind the BM@N facility. This target station has an advantage to use beams for applied research purposes in parallel with operation of the BM@N setup.

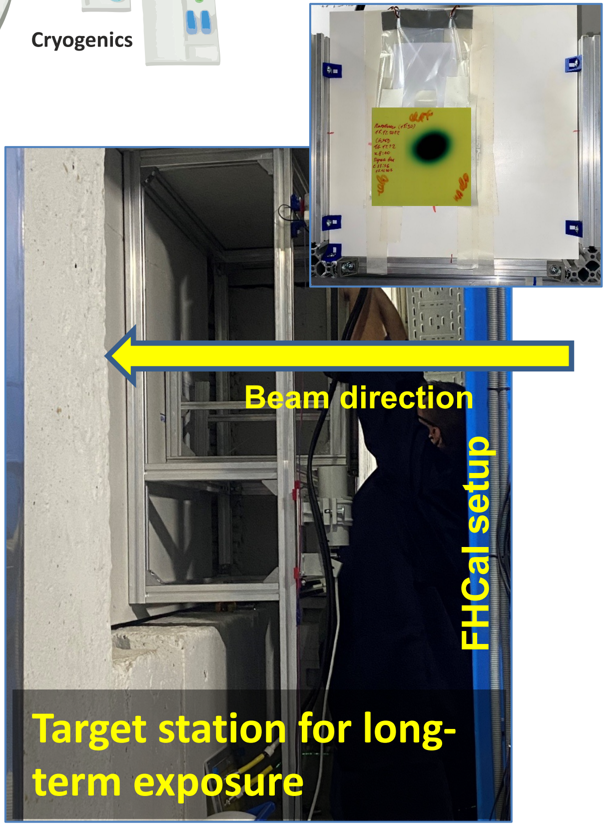


Other ARIADNA beamlines for applied research are in progress



Station Of CHip Irradiation (SOCHI)

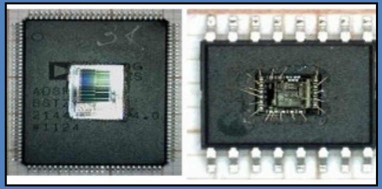
SIMBO and ISCRA target stations



Target station for long-term exposure

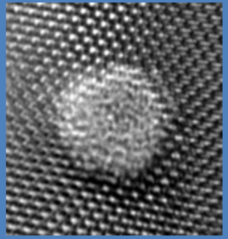
PILLARS OF THE APPLIED RESEARCH PROGRAMME AT NICA

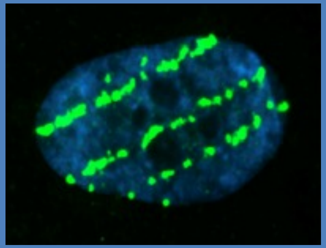
Radiation effects in microelectronics



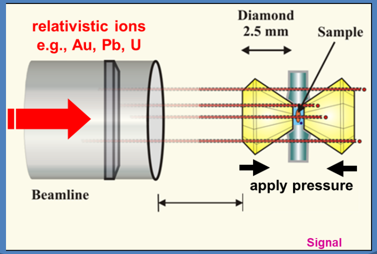
Radiation protection in space

Materials research with ion beams

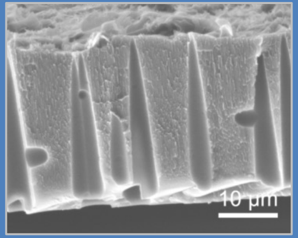


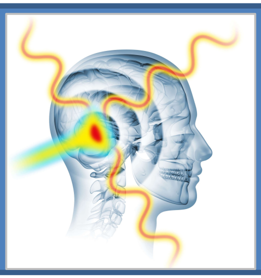


Radiation biophysics and radiobiology

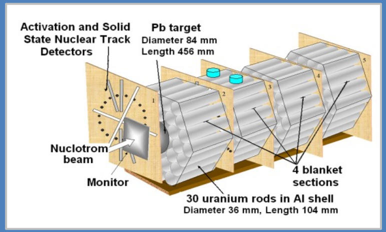


Materials in extreme radiation dose conditions





Radiation therapy-related research



Novel technologies for accelerator-driven systems (ADS)

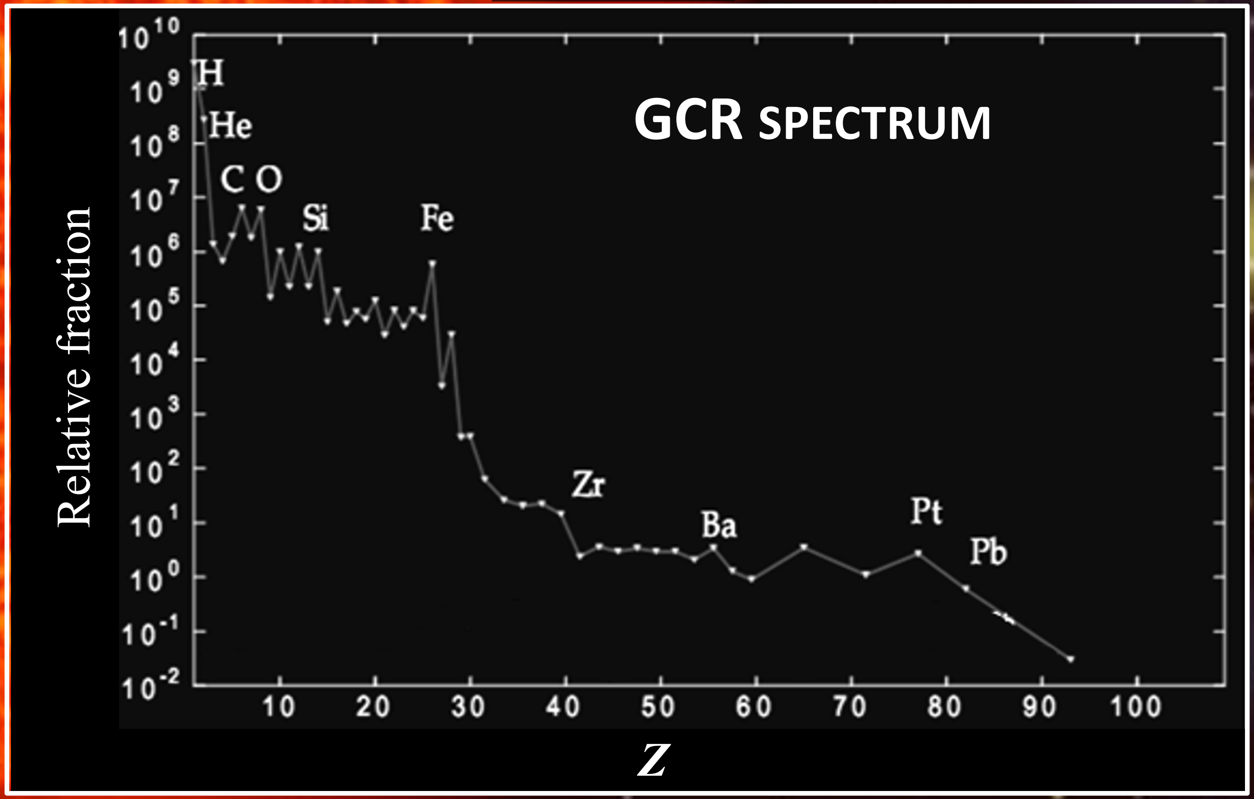
THE ENTIRE SCOPE OF RESEARCH IS NOT LIMITED TO THESE DIRECTIONS AND OPEN FOR USER PROPOSALS

SIMULATION OF SPACE RADIATION COMPONENTS: GALACTIC COSMIC RAYS

Space radiation environment has 2 sources/types

- Galactic Cosmic Rays (GCR) have atomic # 1≤ Z ≤ 92 and energies ~100s of MeV/nucleon and higher (shielding ineffective)
- Solar Particle Events (SPE) have # 1≤ Z ≤ ~26 and energies up to ~10s of MeV/nucleon (shielding can be effective)

Charge

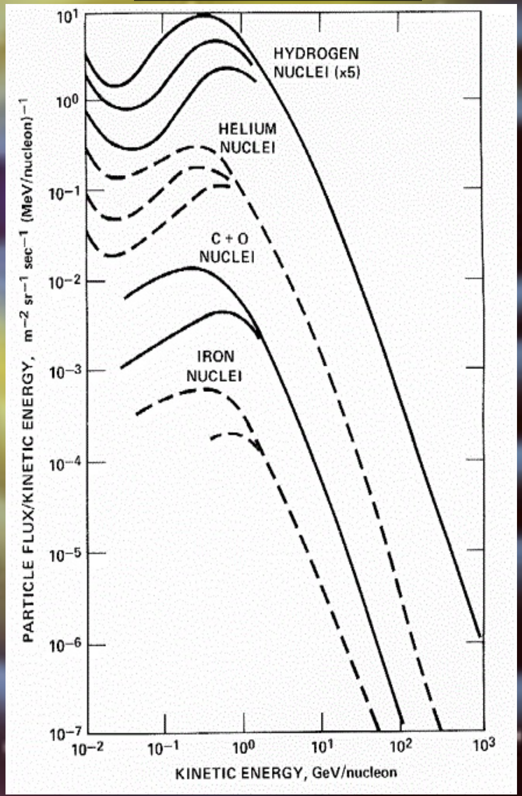


Protons (Z = 1) ~ 92%
He ions (Z = 2) ~ 7%
Ions with c Z = 3÷5 ~ 0.1÷0.15%
Ions of Z = 6÷9 ~ 0,5%
Ions of Z = 10÷15
Ions of Z = 16÷26 ~ 0.065%
Fe ions (Z = 26) ~ 0.025%

Wide range of energies up to 10^{20} eV

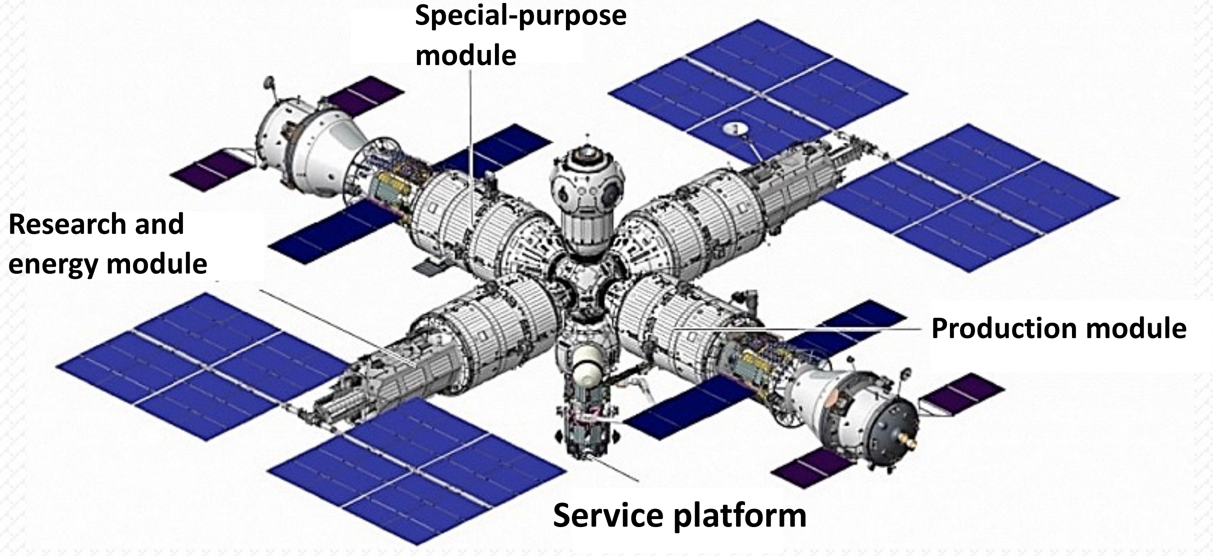
/Dorman, 1975; Kalmykov et al., 2007/

Energy

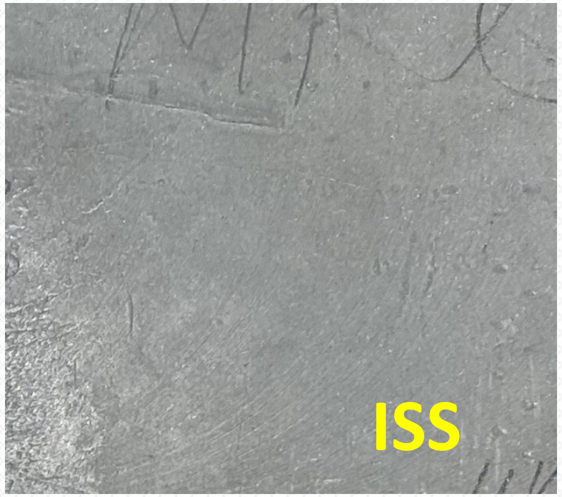


Space Research work package: New composite materials for space industry (protective properties, radiation resistance, radiation-induced modification)

- Improving the regular means of radiation protection in spacecrafts for orbital flights and missions beyond the Earth magnetosphere.
- Study of shielding properties of existing and new composite materials.
- Investigation of radiation modification of composite materials by high-energy accelerated ion beams during long-term irradiation.

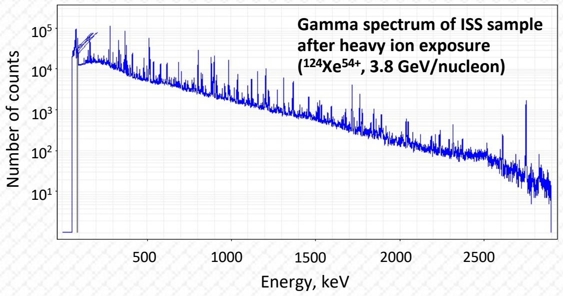


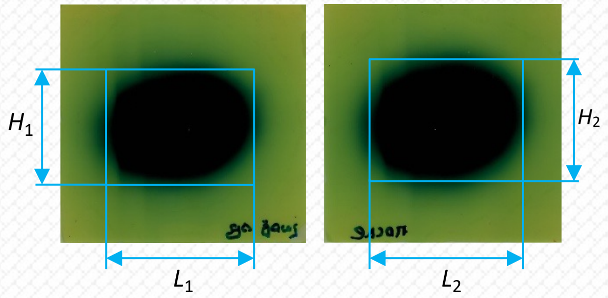
Project of the new Russian Orbital Service Station (ROSS)



Shielding material from the International Space Station (ISS)

New shielding material for the future Russian Orbital Service Station (ROSS)





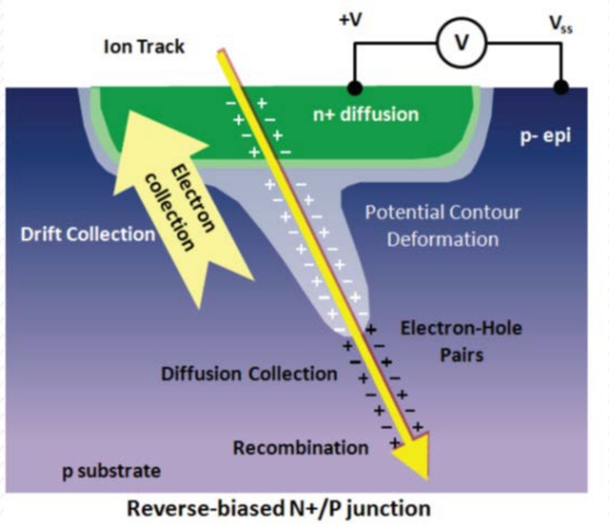
- ❑ Structural, chemico-physical methods of research and testing.
- ❑ Comparative studies under the influence of other types of ionizing radiation.

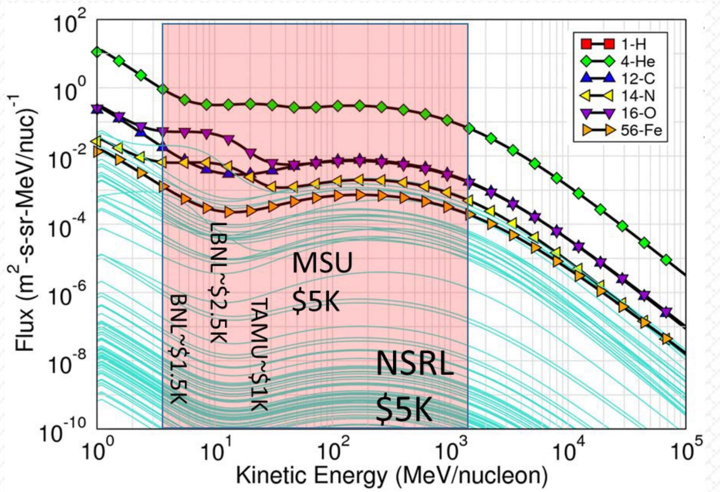
RADIATION TESTING OF ELECTRONICS WITH IONS OF RELATIVELY HIGH ENERGY

Two types of radiation effects

- Cumulative (dose) effects result from long-term exposure to radiation environment
- Single-Event Effects (SEE) occur promptly due to a **single particle** strike

Recent studies: 25-50% of spacecraft anomalies due to SEE (depends on spacecraft orbits)



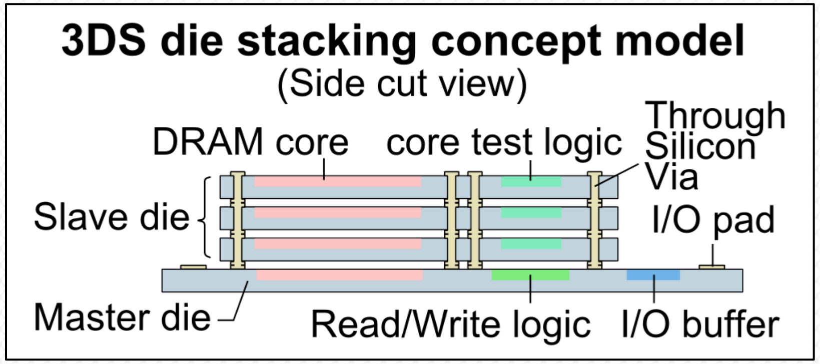


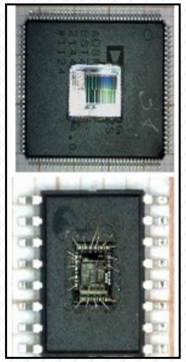
/R.C. Baumann, 2013 NSREC Short Course/

Increasing integration poses problems for SEE testing with low-energy beams

- Multiple die stacked together in packages.
- Behavior may differs if dis-assembled, tested separately.
- Packages now intrinsic to part performance.
- Dis-assembly may compromise timing, thermal and structural characteristics—especially if thinning required.

- Ideally, prefer test with ions' characteristic relevant to space
- GCR ions fairly flat out to >2 GeV/nucleon (min. ionizing)
- Difficult and expensive to achieve at accelerators





/By R.L. Ladbury at the Meeting of the American Physical Society, Columbus, OH, April 14-17, 2018/

SEE Frontiers:

1. Technology Frontier
2. Low-Energy Frontier
3. **High-Energy Frontier – relevant to facilities like NICA**

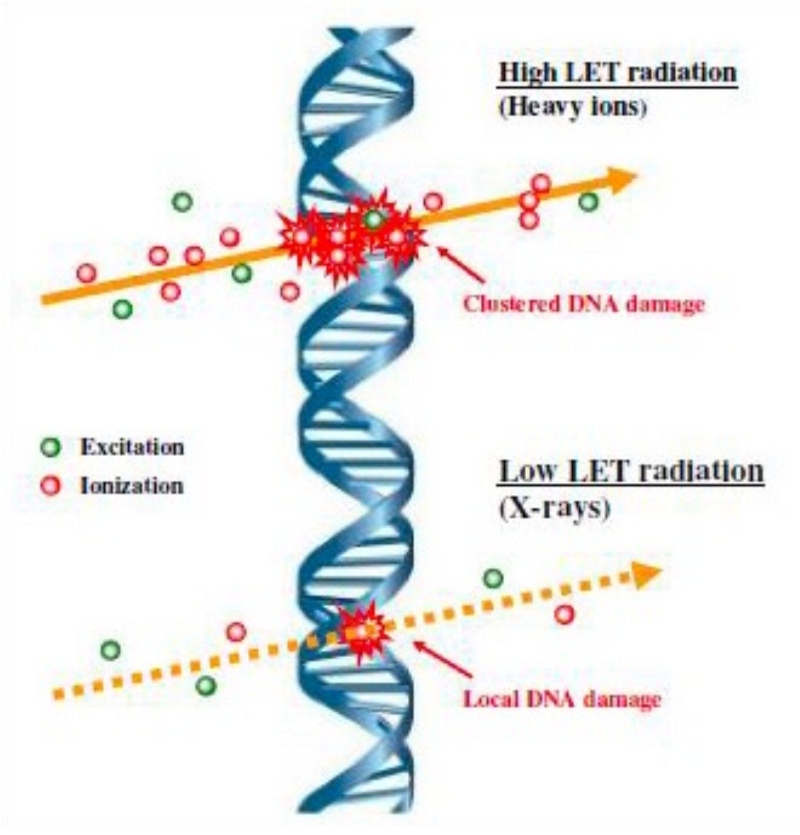
Sample activities of the Life Sciences working package

- Molecular biology research (DNA damage and repair)
- Radiation genetics (gene and structural mutations)
- DNA repair protein biomarkers
- Aspects of the radiation-induced cell death (apoptosis, necrosis)
- Formation of chromosomal aberrations
- Different aspects of radiation-induced cancerogenesis
- Central nervous system disorders following the radiation exposure
- Development of radiation protection measures
- Improvement of beam delivery and dosimetry methods for radiotherapy
- ...

DNA REPAIR PROTEIN MARKERS FOR CANCER CHARACTERIZATION

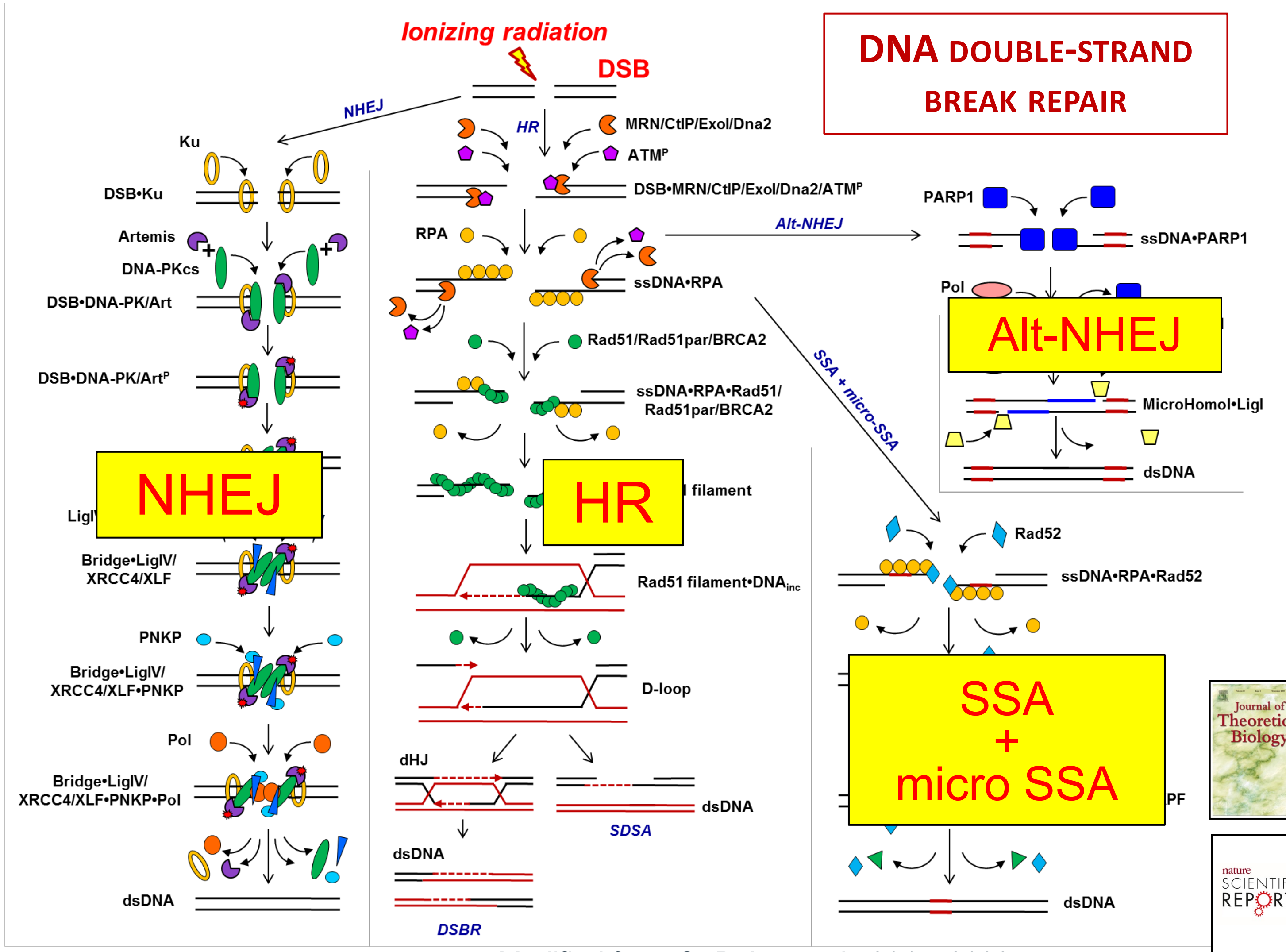
Studying the mechanisms and regularities of DNA repair in normal and cancer cells exposed to different types of radiation exposure (including ion beams produced by NICA facility) enables to identify specific protein markers associated with cancer.

RADIATION-INDUCED DNA DAMAGE



Modified from W. Tinganelli and M. Durante. Carbon Ion Radiobiology. Cancers 2020, 12, 3022

DNA DOUBLE-STRAND BREAK REPAIR



Modified from O. Belov et al., 2015–2023

DNA REPAIR PROTEIN MARKERS FOR BREAST CANCER CHARACTERIZATION

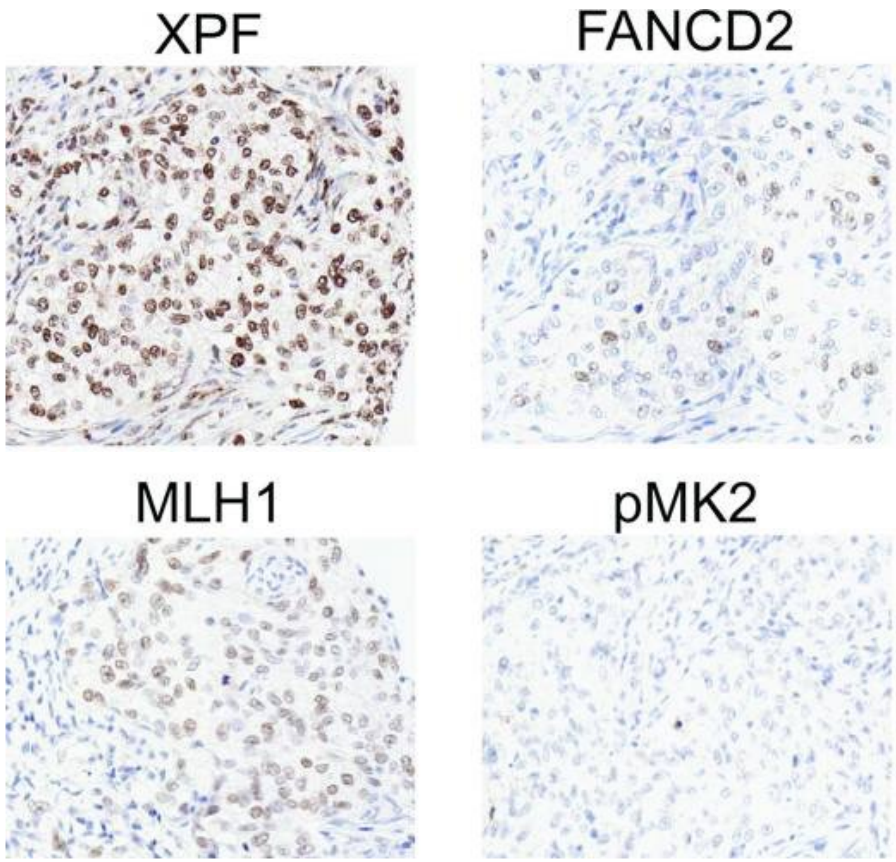
An example is the characterization of the ***triple-negative breast cancer (TNBC)*** being a kind of breast cancer that does not have any of the receptors that are commonly found in this type of cancer. It is estrogen receptor (ER) negative, progesterone receptor (PR) negative and HER-2 low by immunohistochemistry or fluorescent in-situ hybridization.

The characterization method is based on determining the levels of several DNA repair proteins using specific antibodies against proteins in multiple DNA repair pathways. Possible set of antibodies :

XPF — nucleotide excision repair (NER),
FANCD2 — Fanconi Anemia/homologous recombination (FA/HR),
MLH1 — mismatch repair (MMR),
pMK2 — MAPKAPKinase2, DNA damage response (DDR).

The DNA repair patterns exhibiting low XPF, pMK2, MLH and FANCD2 can be associated with shorter time to recurrence of the breast cancer.

A 4-antibody model is suggested to be able to segregate high risk and low risk groups based on time to recurrence of TNBC.

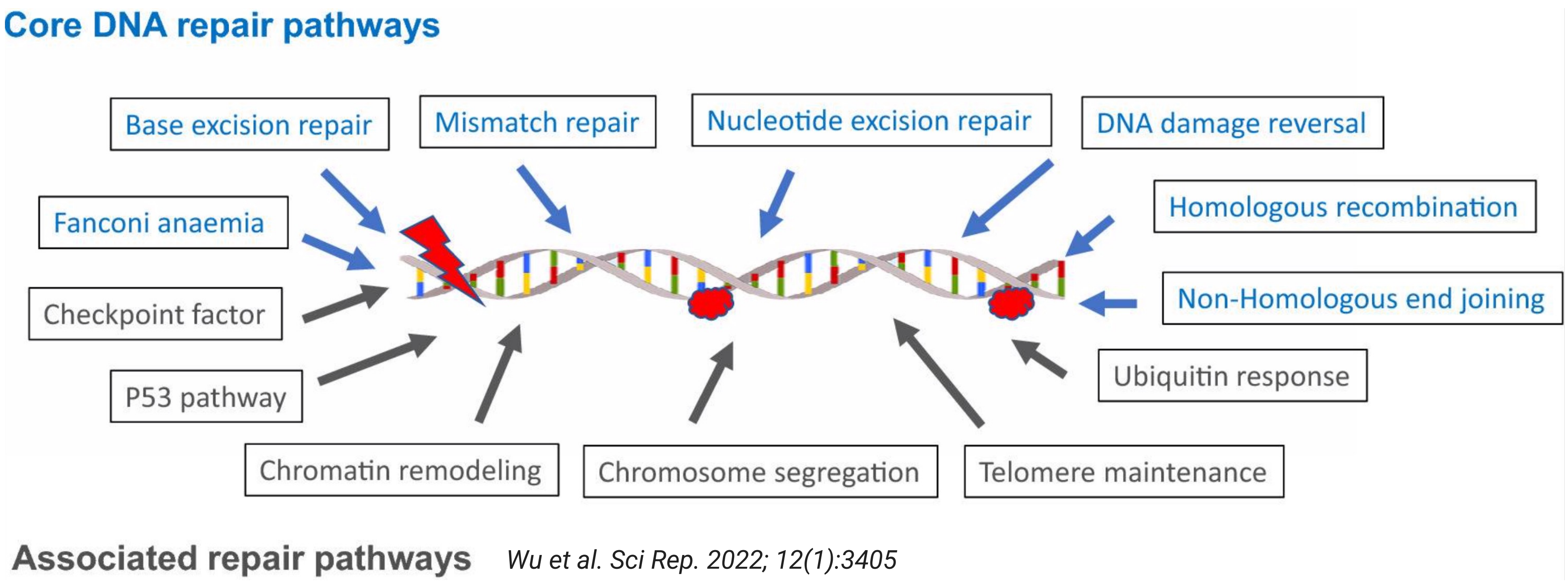


Immunohistochemistry patterns for the several DNA repair antibodies in one triple negative breast tumor

Alexander et al. Clin Cancer Res. 2010; 16(23):5796-804

SEEKING FOR OVERALL PATTERNS OF DNA REPAIR IN DIFFERENT CANCER CELLS FOR FURTHER USE IN PREDICTION AND DIAGNOSTICS

Defining the DNA repair patterns both in its native form and following the exposure to ionizing radiation



Wu et al. Sci Rep. 2022; 12(1):3405

STUDY OF BEHAVIORAL AND NEUROCHEMICAL OUTCOMES IN LABORATORY ANIMALS FOLLOWING APPLICATION OF CHEMICAL AND/OR RADIATION FACTORS

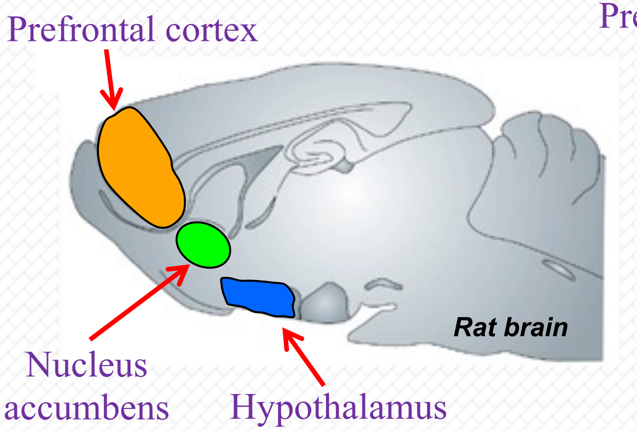
(Both for space-related research and for or preclinical studies using animals to investigate the potential of a therapeutic drug or strategy)

Probing the variety of behavioral reactions in laboratory animals following application of chemical and/or radiation factors:
- **— anxiolytic-/anxiogenic-like effects;**
- **— sedative effects;**
- **— depression model;**
- **— locomotor activity;**
- **— memory;**
- **— stress-vulnerability, etc.**

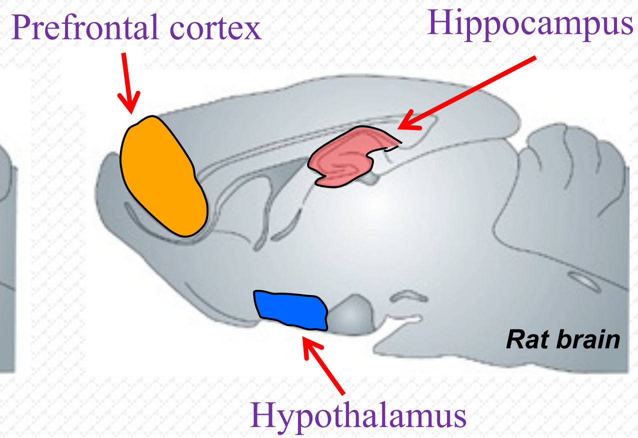
Application of behavioral test sets:
- — Open Field;
- — Elevated Plus Maze;
- — Rotarod Performance Test;
- — Passive Avoidance Task;
- — etc.

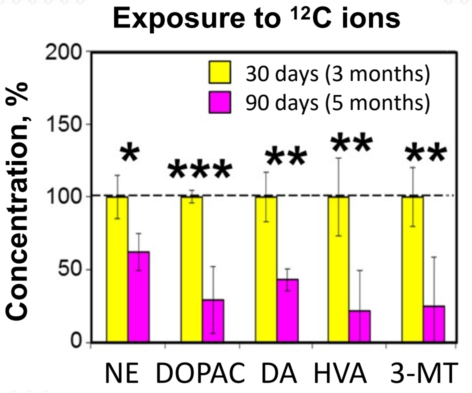
Belov et al., 2015-2022

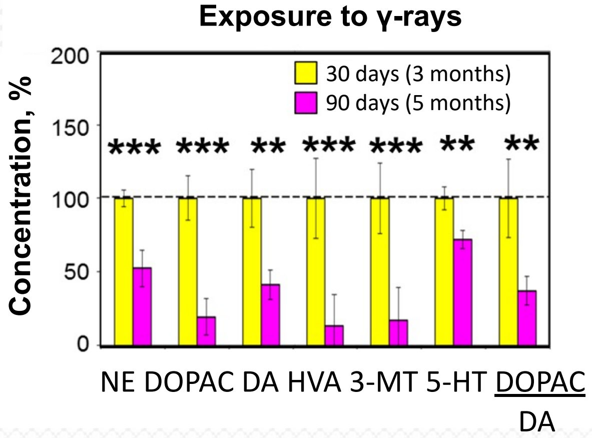
Ions
(^{12}C, 500 MeV/n, 1 Gy)



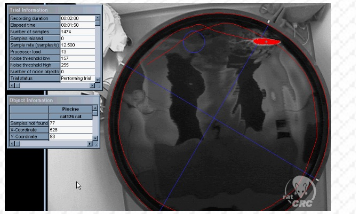
γ-rays
(^{60}Co, 1 Gy)

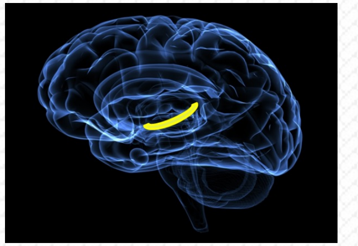






Seeking for most radiosensitive brain structures



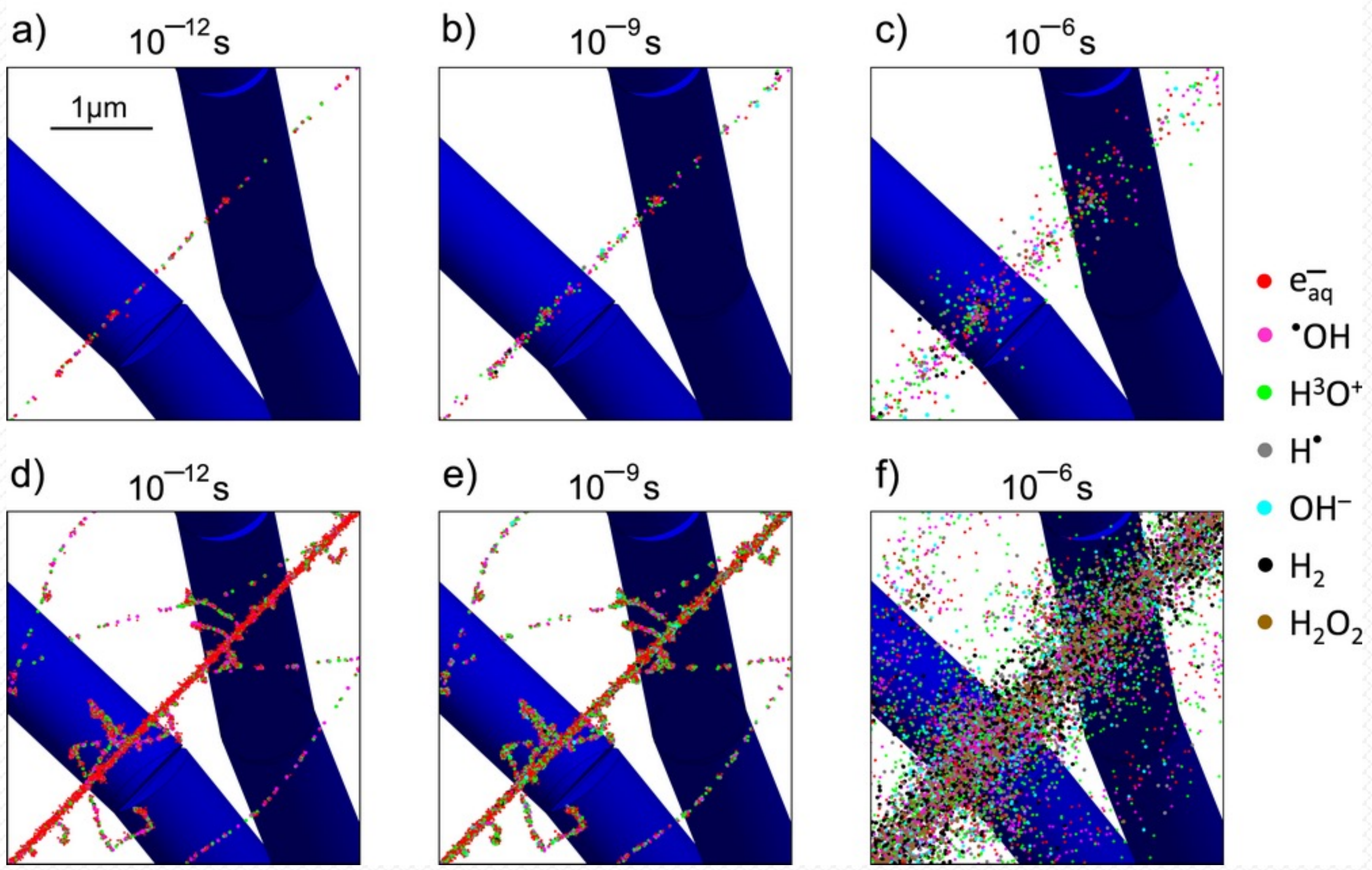


STUDY OF RADIOLYTIC DAMAGE TO NEURAL CELL STRUCTURES

DISTRIBUTION OF FREE RADICALS IN A SINGLE PYRAMIDAL NEURON AFTER IRRADIATION

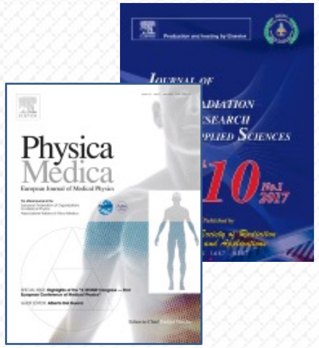
30 MeV ^{+}p particle track →

1000 MeV/u ^{56}Fe particle track →



Track structure of a 30 MeV proton and 1000 MeV/u ^{56}Fe ion in dendritic branches of pyramidal neuron, as viewed at picosecond, nanosecond, and microsecond after exposure

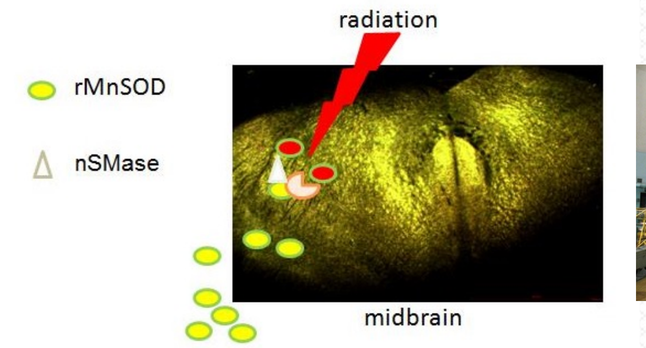
Experimental verification is needed!



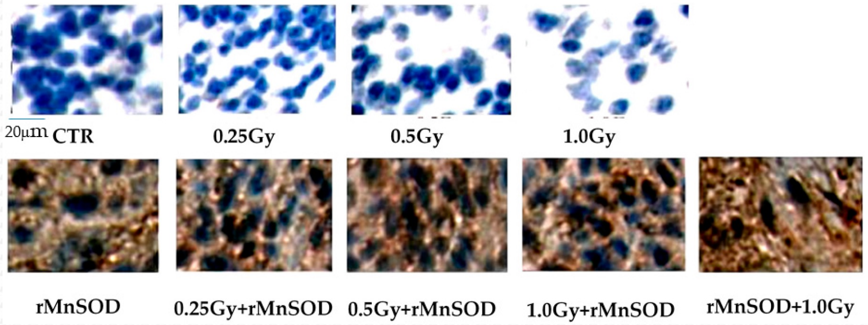
Belov et al., 2019-2021

Radiation protection frontier

Development and testing of pharmaceuticals for protecting astronauts from space radiation on experimental models of laboratory animals



It has been established that recombinant human manganese-containing superoxide dismutase (rMnSOD), which has specific antioxidant and antiradical activity, is able to overcome the blood-brain barrier and penetrate into the midbrain, preventing radiation damage.

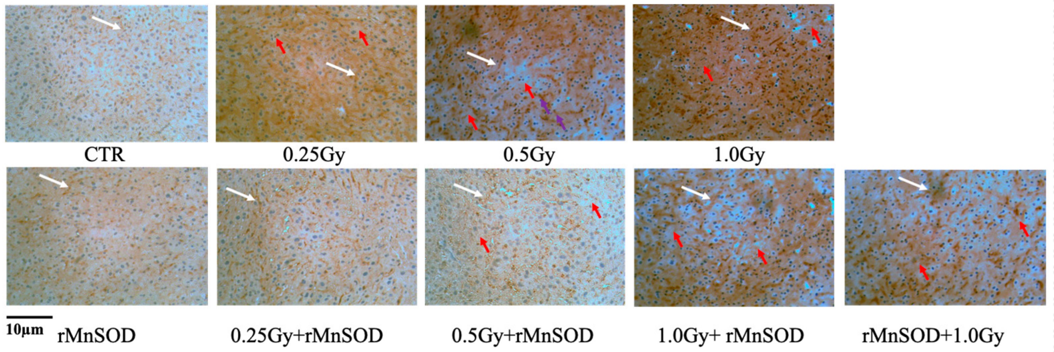


Localization of rMnSOD in brain tissue. Immunohistochemical analysis was performed by using specific antibody. The immunostaining was evident only in brain samples from rMnSOD-treated mice.

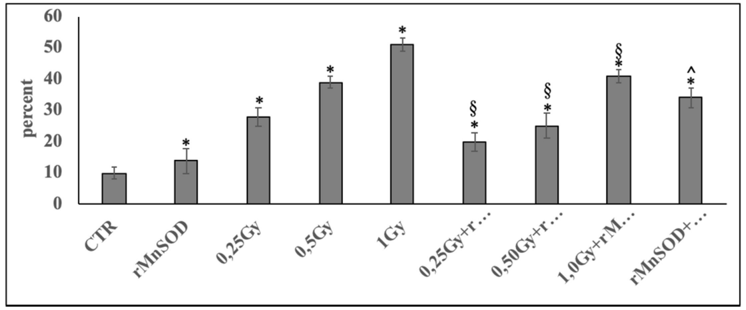
Cataldi, S.; Borrelli, A.; Ceccarini, M.R.; Nakashidze, I.; Codini, M.; Belov, O.; Ivanov, A., et al. Neutral Sphingomyelinase Modulation in the Protective/Preventive Role of rMnSOD from Radiation-Induced Damage in the Brain. Int. J. Mol. Sci. 2019, 20, 5431.

The ability of rMnSOD to reduce radiation-induced damage has been shown, both through a protective role associated with sphingomyelinase with an acidic pH optimum (aSMase), and through a prophylactic role through sphingomyelinase with a neutral pH optimum (nSMase).

a)



b)

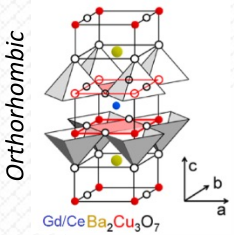


Mouse liver after irradiation with or without protective or preventive rMnSOD treatment (**a**) representative liver histology by Caspase-1 immunohistochemical staining. (**b**) Quantification of Caspase-1 staining was performed using the ImageFocus software. Positive staining is indicated as low (+), medium (++), or high (+++). Only high positive staining was considered and was measured as a percentage of the total area. Data represent the mean + S.D. of three livers for each group. Significance, * $p < 0.05$ with respect to the CTR, § $p < 0.05$ with respect to the irradiated samples, ^ $p < 0.05$ with respect to 1.0 Gy + rMnSOD.

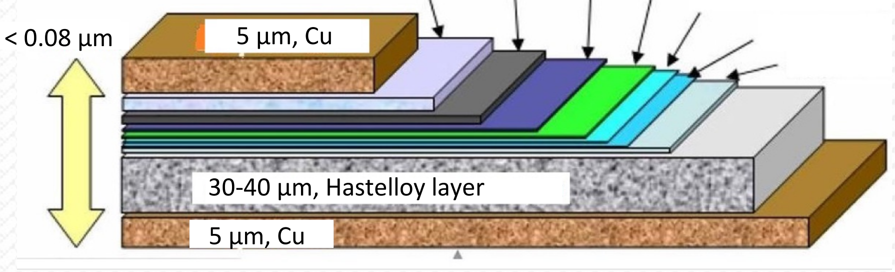
Cataldi S, Borrelli A, Ceccarini MR, Nakashidze I, Codini M, Belov O, Ivanov A, et al. Acid and Neutral Sphingomyelinase Behavior in Radiation-Induced Liver Pyroptosis and in the Protective/Preventive Role of rMnSOD. Int J Mol Sci. 2020, 21(9), 3281.

Materials Science working package: Irradiation of high-temperature superconducting tapes

- Development of methods for increasing the critical current of high-temperature superconductors (HTSC) by means of radiation modification (induction of pinning centers in the bulk of the superconductor).
- Comparative analysis of the critical current values upon irradiation of HTSC tapes with $^{124}Xe^{54+}$ ions of 3.8 GeV/nucleon and protons of 660 MeV.
- Estimation of the stability of the effect of increasing the critical current in an irradiated superconductor.
- Development of equipment prototypes based on radiation-modified HTSC tapes and their testing.



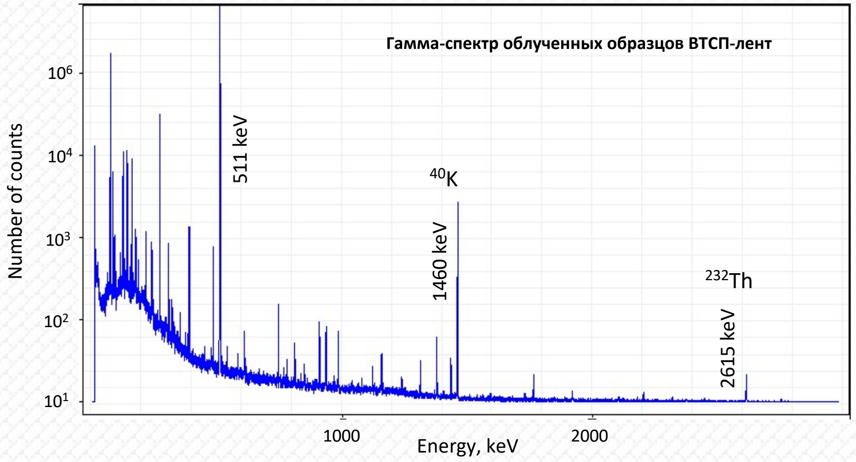
HTSC tape structure

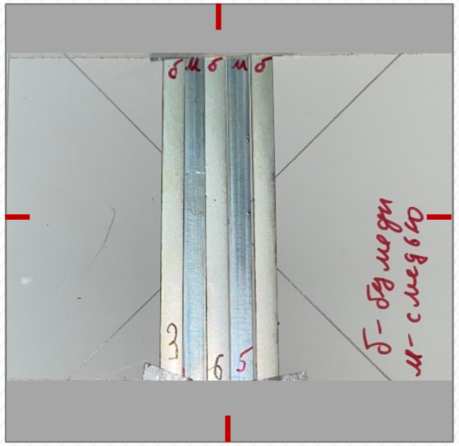


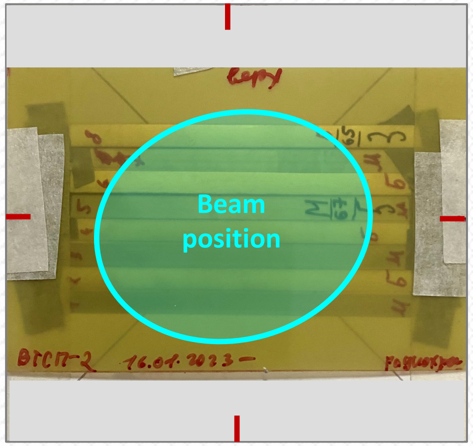
0.1-0.2 mm

Methods for measuring current-voltage characteristics, Hall coefficient, magnetoresistance, thermo-EMF coefficient, thermal conductivity coefficient, magnetic moment in the temperature range of 1.7–300 K and magnetic fields up to 8 T.

Irradiation of vertically and horizontally arranged HTSC tapes with and without copper content





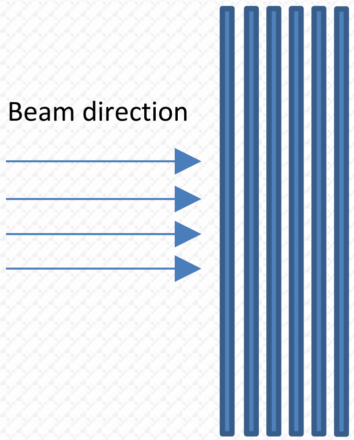


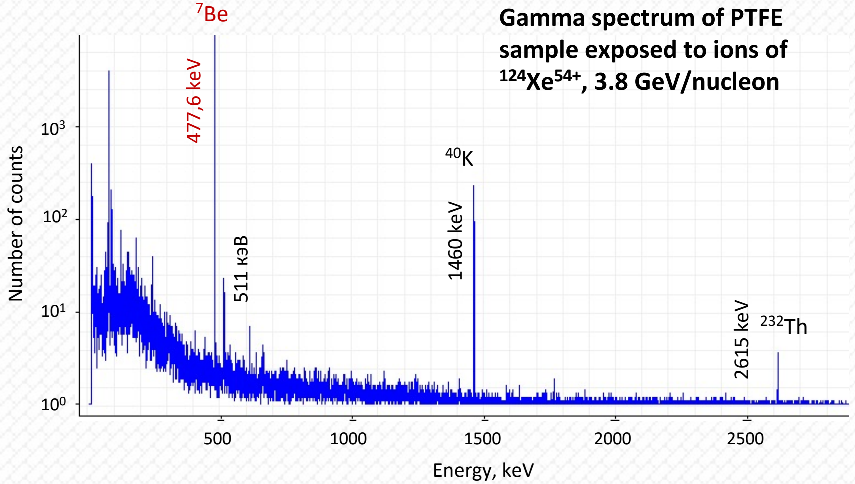
TSC tapes manufactured by "SuperOx" LLC

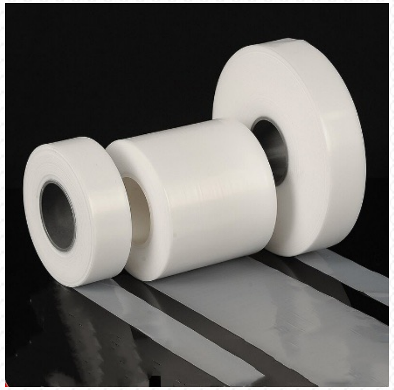
Radiation modification of polytetrafluoroethylene (PTFE), polyethylene terephthalate (PET), polyethylene (PE) and polyimide (PI) films

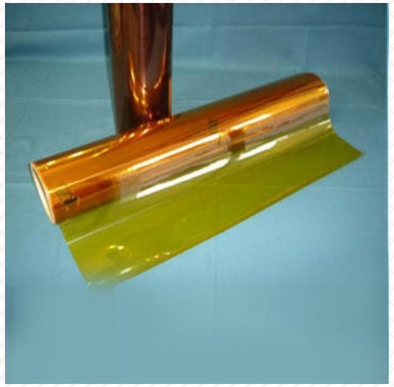
- Study of the processes of amorphization and recrystallization of polymers and nanocomposite materials.
- Investigation of regularities of radiation-chemical damages in PTFE, PET, PE and PI films.
- Establishment of regularities in radiolysis of condensed matter under the exposure to ion beams with energies of several GeV/nucleon.
- Development of ion-track technologies with "thick" targets and multilayer materials.

Multilayer film packs for exposure









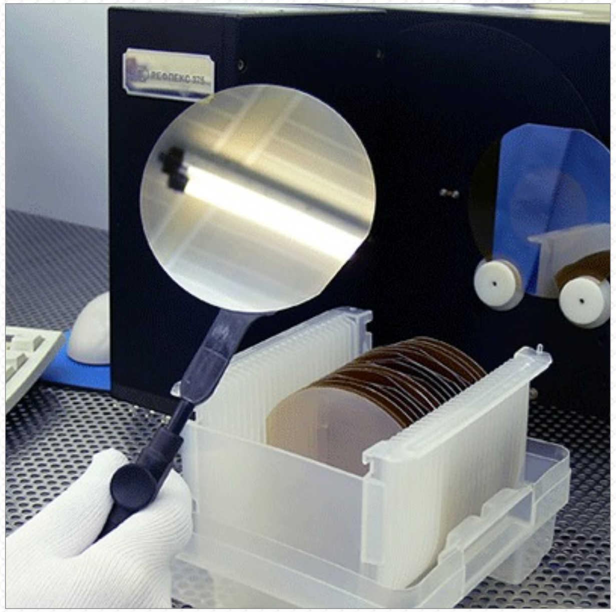

PTFE, PET, PE and PI films of 12, 20, 40, 50, 80 µm thick

Research methods: scanning and transmission electron microscopy, X-ray phase analysis, X-ray photoelectron spectroscopy and X-ray energy-dispersive elemental analysis, atomic force microscopy and low-temperature nitrogen sorption, wettability with respect to water and heptane, optical and infrared spectroscopy, infrared spectroscopy of frustrated total internal reflection, diffuse spectroscopy and specular reflection, laser Doppler strainmetry.

STUDY OF RADIATION MODIFICATIONS IN SAPPHIRES (Al_2O_3)
AS A RESULT OF THE LONG-TERM HEAVY ION EXPOSURE

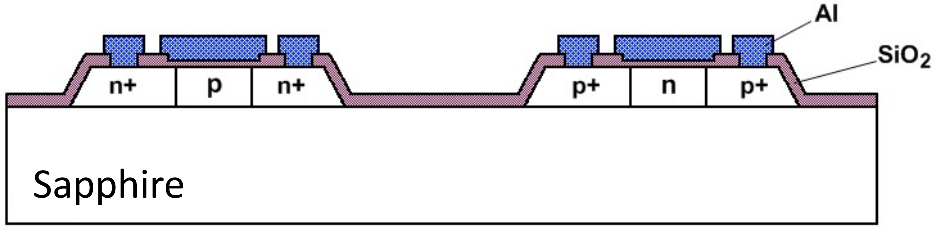
Study of structural modifications and the state of matter as a result of the accelerated ion beam exposure of on sapphires (Al_2O_3).

Improvement of the "silicon on sapphire" technology in topics assuming the impact of relatively high-energy ions (deep space, radiation-resistant electronics for charged particle accelerators, etc.).

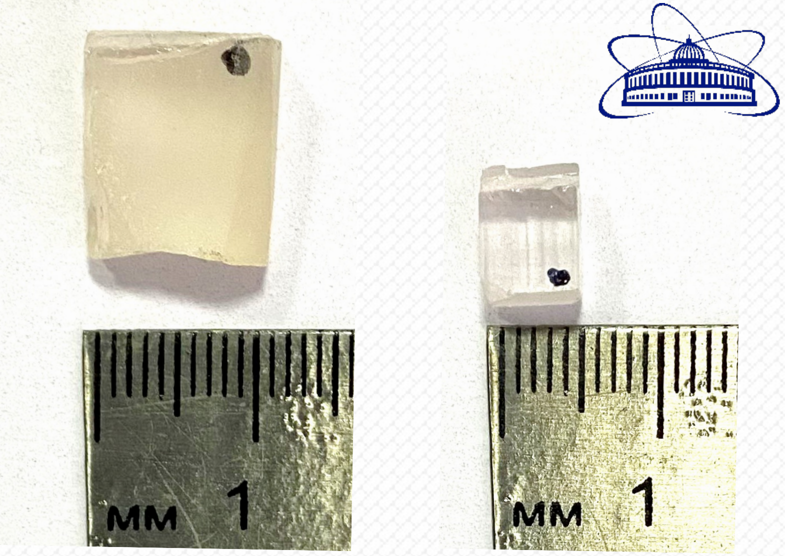


Research methods used:
atomic force microscopy; scanning electron microscopy; electron spectroscopy for chemical analysis; X-ray fluorescence analysis; mass spectrometry; thermal analysis.

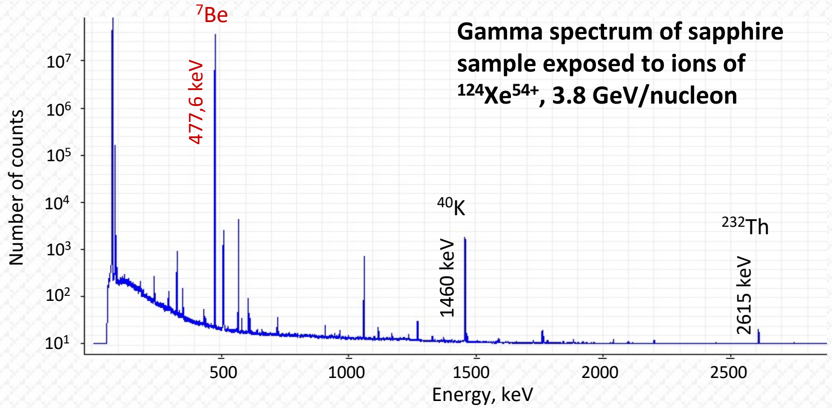
”Silicon on sapphire" (SOS) technology



Samples of sapphires*

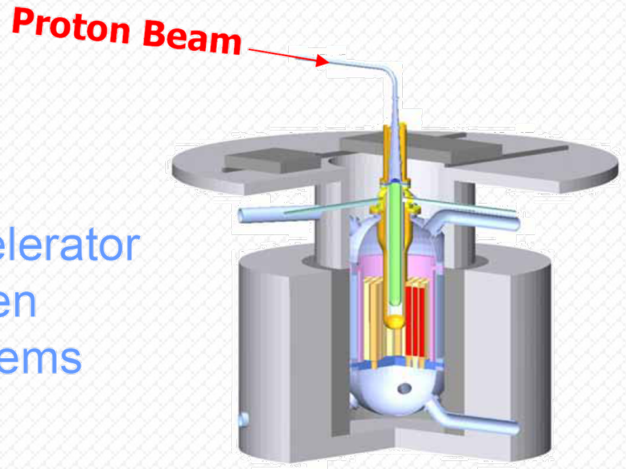


*Transparent wedge-shaped samples of crystalline alumina (sapphire) produced by the Vernel method.



Novel nuclear technologies with NICA beams

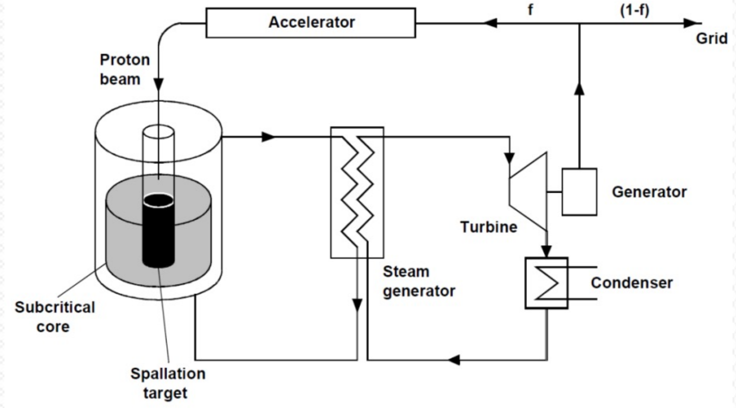
Accelerator Driven Systems (ADS) are the nuclear systems based on interaction of particle beams extracted from the accelerator with deeply subcritical quasy-infinite active zones consisting of the depleted (natural) uranium, thorium and spent nuclear fuel.



Accelerator Driven Systems

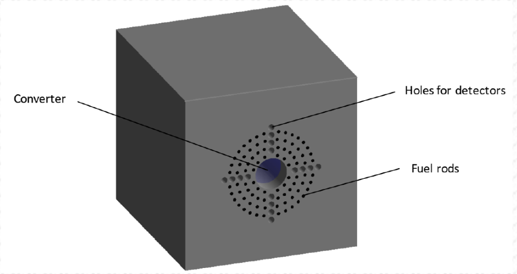
In previous years, the conditions which maximize the efficiency of ADSR were investigated. The optimal value of criticality coefficient of the core k_{eff} is in the range 0.985 - 0.988. It was suggested that the best choice for the converter is Be, especially for ion beams at low energy.

The maximum energy gain of protons is obtained at 1.5 GeV when they are accelerated in a LINAC, and at lower energy (0.75-1 GeV) when a cyclotron is used. In both situations ion beams starting with ^{4}He realize higher energy gain than protons. When particles are accelerated in a LINAC, at low accelerator length a beam of ^{7}Li with energy 0.25 AGeV represents the best option.

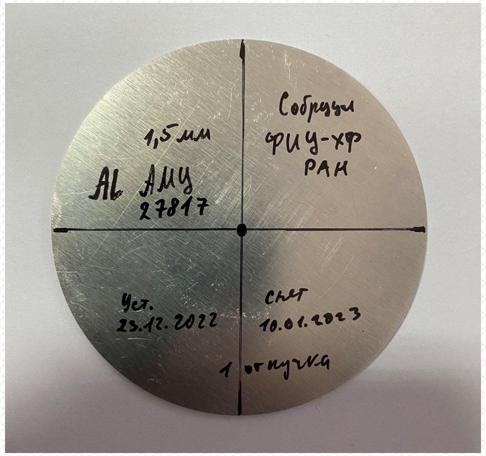


Within the next years the ADSR project will be concentrated on:

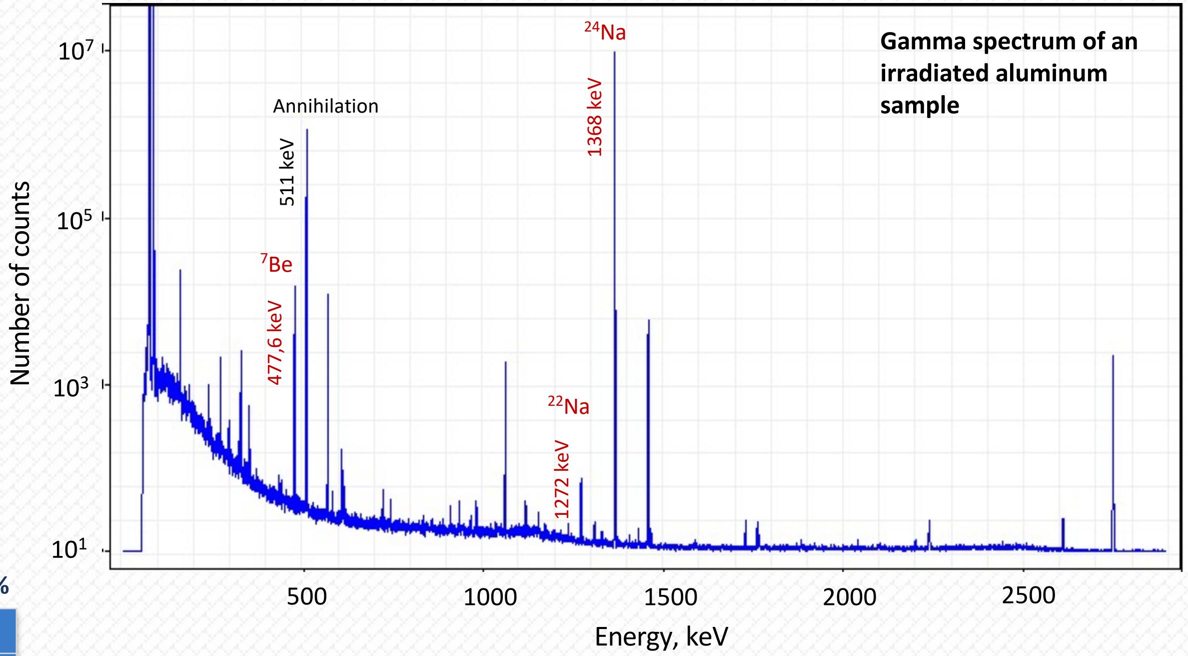
- **Research activities, involving simulation study, on an optimal design of the target;**
- **Verification of a principally new concept of a system based on the use of ion beams instead of protons;**
- **Implementation of the first stage of experimental program focused on measurement of the neutron yields with different converter combinations.**



Activation analysis of materials upon irradiation with $^{124}Xe^{54+}$ ions of 3.8 GeV/nucleon

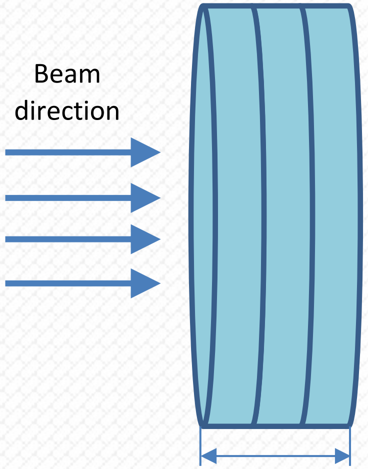


Aluminum target
АМЦ 27817 (1.5 x Ø70 мм)



Composition (GOST), %

Al	96.35 — 99
Mn	1 — 1.5
Cu	0.05 — 0.2
Fe	Up to 0.7
Si	Up to 0.6
Zn	Up to 0.1



Al, 1.5 x 3 = 4.5 мм

Spectrometer of gamma radiation SEG-1KP-IFTP (detection unit BDEG-OGK-3K)

ARIADNA COLLABORATIONS FOR APPLIED RESEARCH AT NICA

ARIADNA-LS Collaboration	ARIADNA-MSTE Collaboration	ARIADNA-NPT Collaboration
The Collaboration is being established in order to perform experiments in the field of life sciences at the NICA Complex with the ARIADNA beamlines	The Collaboration is being established in order to perform activities and experiments in radiation materials science and radiation testing of electronics at the NICA Complex with the ARIADNA beamlines	The Collaboration is being established in order to facilitate novel developments for nuclear technology at the NICA Complex with the ARIADNA beamlines

Collaborating organizations

1. Joint Institute for Nuclear Research (Dubna, Int.)
2. Institute of Biomedical Problems, RAS (Moscow, Russia)
3. Burnasyan Federal Medical Biophysical Center of Federal Medical Biological Agency (Moscow, Russia)
4. Skobeltsyn Research Institute of Nuclear Physics, Moscow State University (Dubna, Russia)
5. Saint Petersburg State University (Saint Petersburg, Russia)
6. Tsyb Medical Radiological Research Centre (Obninsk, Russia)
7. Semenov Research Center of Chemical Physics, RAS (Moscow, Russia)
8. Institute of Theoretical and Experimental Biophysics, RAS (Moscow, Russia)
9. Moscow Institute of Physics and Technology (Dolgoprudny, Russia)
10. Kurnakov Institute of General and Inorganic Chemistry, RAS (Moscow, Russia)
11. National Research Nuclear University MEPhI (Moscow, Russia)
12. Joint Institute of High Temperatures, RAS (Moscow, Russia)
13. North Ossetian State University (Vladikavkaz, Russia)
14. Institute of Nuclear Problems of the Belarusian State University (Minsk, Belarus)
15. Institute of Nuclear Physics, AS RUz (Tashkent, Uzbekistan)
16. LLC Research and production company “Kvant-R” (Moscow, Russia)
17. LLC “S-Innovations” (Moscow, Russia)
18. LLC “SOL-Instruments” (Minsk, Belarus)
19. IC CANDLE, Yerevan, Armenia
20. Yerevan State University, Yerevan, Armenia

157 participants

ARIADNA ACCESS

- Both academic and industrial groups are eligible to access the ARIADNA infrastructure.
- A correspondingng user policy at NICA is under development, which includes regulations on equipment use, bioethics, access to beamlines and to supportive user infrastructure, etc.
- Funding opportunities can also be provided on the basis of special-purpose grant programs launched for NICA by external funding agencies.
- Main counterpart from ARIADNA users: results need to be published!




Ways of getting involved in ARIADNA

- As a **member of ARIADNA collaboration:** get in touch with us and we will provided instructions on signing an MoU to become a member of the collaboration.
- As a **user:** just prepare and submit you proposal for consideration.
- As an **ARIADNA partner:** let us know how you think you/your research team or company can contribute to ARIADNA and we can prepare a relevant application to be discussed with NICA management.

Thank you for your attention

Contact information:

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Joint Institute for Nuclear Research

E-mail: oleg.belov@jinr.int, dem@jinr.ru