Приложение 2

**Questionnaire**

for the extraordinary session of the PAC for Condensed Matter Physics for the assessment of related JINR projects

**Project: “Further development of methods, technologies, schedule modes and delivery of radiotherapy”**

**Theme 02-4-1132-2017/2022**

**Project Leader: G.V. Mytsin**

**PART A: Achievements**

1.   Contributions of the JINR group:

-List the contributions of the JINR group in hardware (including use of JINR computing resources for the project), software development and physics analyses

**The technique of 3-D conformal proton radiotherapy of deep seated tumours was realized at the Medico-Technical Complex of DLNP JINR for the first time in Russia and Eastern Europe.**

**The members of JINR group developed a unique software for the treatment planning of 3-D conformal proton radiotherapy, a hardware-software complex for verification of a patient position during radiotherapy, a hardware-software complex for verification of boluses individually manufactured for patients proton irradiation.**

**A prototype of a multileaf collimator and an automated range shifter for a new technique of dynamic proton beam irradiation have been constructed and tested.**

-List the responsibilities of JINR group members within the management structure of the collaboration, if any, giving the name of the JINR member, the managerial role and the appointment period.

**Project Leader: G.V. Mysin since 2000 year, also Theme Leader.**

2.   Publications:

-List the papers published in the refereed literature (no conference proceedings) in which the JINR group had a major contribution (e.g. author of the analysis, promoter of the experiment, corresponding author, realization of a key equipment etc.). Give title of paper, reference and describe in 1-2 sentences the JINR contribution. Only papers published since the last approval of the project should be listed.

**1. Shipulin K. N., Mytsin G. V. A 3D planning program for proton therapy. Medical Physics, 3(87), 9-26. 2020. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**2. Shipulin, K. N. Automated verification of patient’s positioning in conducting conformal proton radiation therapy. Medical Physics, 2(82), 38-43. 2019. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**3. Agapov A.V., Gaevsky V.N. et al. Experience in the use of proton radiation therapy at the Joint Institute for Nuclear Research, Dubna. Medical Radiology and Radiation Safety. 2019, Vol. 64 (No 2), 61-69. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**4. Agapov A.V., Mytsin G.V. Design of а Multileaf Collimator for Proton Therapy Goals. Medical Physics, № 1 (85), 2020, 9–10. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**5. Agapov A.V., Mytsin G.V. A Multileaf Collimator for Proton Radiotherapy. Biomedical Engineering. № 54 (6), 2021, 407-410. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**6. А. Agapov, G. Mitsyn. Technique of Dynamic Irradiation for Proton Radiotherapy. Meditcinskaya Tehnika. №2, 2021, 45–49. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**7. А.V. Rzyanina, G.V, Mytsin et al. Enhancement of genotoxic activity of gamma-irradiation of human lung carcinoma A 549 cells in the presence of gold nanoparticles. Medical Physics, № 1 (89), 2021, 37-38. The work was fully done by the JINR group members at the Medico-Technical Complex of DLNP.**

**8. D. Sakata, O. Belov et al. Fully integrated Monte Carlo simulation for evaluating radiation induced DNA damage and subsequent repair using Geant4-DNA. Nature Scientific Reports. 2020, Vol. 10, Article 20788. Major contribution of the JINR party is done via suggesting a key idea for future extension of the Genat4-DNA project towards simulation of DNA repair. Author from JINR also developed the corresponding biological prediction model of the DNA double-strand break repair, integrated it into the Geant4-DNA, developed and discussed the validity of the model.**

**9. O. Belov, K. Belokopytova, A. Bazyan. On Molecular and Cellular Mechanisms of Radiation-Induced Damage to Physiological Functions Associated with the Central Nervous System. Successes of physiological sciences (Uspekhi Fiziologicheskih Nauk). 2020, Vol. 51 (2), 3–26. Contribution of JINR team as major authors of analyses and as promoters of radiation neurochemistry experiments discussed in the review. JINR team largely contributed to the drafting the final paper.**

**10. O. Belov, K. Belokopytova et al. Neurochemical insights into the radiation protection of astronauts: distinction between low- and moderate-LET radiation components. European Journal of Medical Physics (Physica Medica). 2019, Vol. 57, 7-16. JINR team was a major developer and promoter of the experiment. Co-authors from JINR were the main participants of the data taking process, dosimetry of proton exposure and also acted as corresponding authors of the resulting paper.**

**11. D. Sakata, N. Lampe et al. Evaluation of early radiation DNA damage in a fractal cell nucleus model using Geant4-DNA. European Journal of Medical Physics (Physica Medica). 2019, Vol. 57, 152-157. Authors from JINR contributed to formulation of simulation approaches relevant for future implementation of DNA double-strand break repair model into the Geant4-DNA.**

**12. V.S. Kokhan, P.K. Anokhin et al. Cortical Glutamate/GABA Imbalance after Combined Radiation Exposure: Relevance to Human Deep-Space Missions. Neuroscience, 2019, Vol. 416, 295-308. Authors from JINR largely contributed to the data analysis with the relevance to the radiation environment of deep-space exploration missions.**

**13. Mianowski S., Borowicz D.M. et al. SiPM proton irradiation for application in cosmic space. JINST, 15, 1-8. 2020. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**14. Lyakhova K.N., Kolesnikova I.A. et al. The effect of the drug "SEMAX" on the life status and morphological changes in the brain of mice under proton irradiation. Radiation biology. Radioecology. 2019, Vol. 59 (No 2), 191-199. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**15. Lyakhova K.N., Kolesnikova I.A. et al. Morphofunctional indicators of the effect of protons on the central nervous system. Medical radiology and radiation safety. 2019, Vol. 64 (No 2), 75-81. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**16. Severyukhin Yu. S., Feldman T.B. Effect of cranial irradiation with 170 MeV protons at a dose of 5 Gy on visual behavior and optomotor response of adult rats. Radiation Biology. Radioecology. 2019, Vol. 59 (No 5), 532-537. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**17. Mitrofanov I. G., Golovin D. V. First Results for Laboratory Tests of a Concept of Space Gamma-Spectrometer with Tagged Protons Method at the JINR Particle Accelerator. Physics of Particles and Nuclei Letters. 2019, Vol. 16 (No 3), 251–255. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**18. Mitrofanov I. G., Litvak M.L. Gamma-spectrometry of composite targets-analogs of planetary matter on the proton beam of the JINR accelerator using the labeled proton method. PEPAN Letters. 2020, Vol. 17 (No 3), 299-313. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**19. Ivanov A.A., Krylov A.R. et al. Modeling of Laboratory Animals Exposure Conditions behind Local Concrete Shielding Bombarded by 650-MeV Protons. Medical Radiology and Radiation Safety. 2020, Vol. 65 (No 5), 77-86. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

**20. Oprica L., Vochita G. et al. The evidence of some biochemical changes in the seedlings grown from proton exposed seeds. Rev. Fiz. Med., 2020, Vol. 8 (No 3), in press. The test samples were irradiated at the therapeutic proton beam of the DLNP Phasotron by the JINR group.**

3.   PhD theses:

-List the PhD theses completed within the last 3 years, or expected to be completed within 2021, by JINR students within the project, giving the student name, thesis title and graduation year.

**1. Cristina Oanchea: “Optimization of proton and carbon ion therapy in presence of metallic implants: dosimetry experiments and Monte Carlo simulations”, PhD dissertation, 2019.**

**2. Konstantin Shipulin: “Development of software and hardware tools for planning and quality assurance of conformal proton radiotherapy”, Candidate of Science, 2021.**

**3. Alexey Agapov: “Development of technical means and methods of dynamic irradiation for proton radiotherapy”, Candidate of Science, is planned in 2021.**

**4. Indira Khassenova: “Dosimetry of the therapeutic proton beam of the JINR Phasotron based on Gafchromic polymer films”, Master’s thesis, 2019.**

4.   Talks:

-List the invited plenary talks given by members of the JINR group at international conferences, workshops… since the last approval of the project: give name and date of the conference, title of talk and speaker name.

-Give a similar list for parallel talks.

**PART B: Plans and requests**

5.   Plans

-Describe the plans of the JINR group within the project, in physics analysis, data taking, software development. detector R&D, detector operation and maintenance, upgrade activities… for the period of time of the requested extension.

***Clinical research:***

* **To carry out a statistical analysis of the results of proton therapy clinical studies on the irradiation of patients with different diagnoses.**

***Development and upgrade of proton therapy methods:***

* **Further development and construction of equipment for dynamic conformal proton beam irradiation of deep seated targets will be continued, including the creation of a computer-controlled moderator of variable thickness and a full-scale version of a multileaf collimator.**
* **It is supposed to design and construct a computerized dose control system for proton therapy.**
* **Work will continue to expand the functionality of the three-dimensional conformal proton radiotherapy planning software being developed at the MTC and its clinical testing in irradiation sessions.**

***Dosimetry and microdosimetry of therapeutic hadron beams:***

* **Activities will be continued on LET spectra measurements of clinical proton beam of DLNP Phasotron with Si detectors Liulin and Medipix.**
* **During radiotherapy, in devices of proton beam forming secondary particles appear, in particular neutrons and photons that irradiate surrounding healthy tissues. Doses from such fields should be minimized as they can lead to negative effects, up to formation of secondary radiation-induced tumours. Work is planned at the medical proton beam of the Phasotron to measure background conditions in the proton therapy room. Such measurements will also be conducted at the scanning clinical proton beam in the Proton Therapy Center in Prague (PTC). The obtained data will be compared with the results of measurements at the proton beam DLNP JINR.**

***Radiobiology:***

* **Continuation of studies to determine the forms of fibroblast cell death depending on the dose of ionizing radiation. To study the lethal effect of laser radiation with a wavelength of 532 nm on the survival of fibroblast cells. In order to clarify the mechanism of radioprotective action of laser radiation (633nm and 532 nm) on biological objects to determine the ratio of forms of death after exposure to ionizing radiation, as well as after the combined effect of ionizing radiation and laser radiation.**
* **Study of the effects of increased cytotoxic effects of radiation therapy in the presence of metallic nanoparticles in animal cells. Determination of characteristics of radiation produced during radiotherapy (with and without nanoparticles) inside cells. These parameters can be calculated with a high degree of accuracy based on measurements with the Timepix-3 detector. Identification of new mechanisms of combined methods of treatment of tumor cells using metal nanoparticles and identification of their role in enhancing the effect of γ-rays and protons on tumor cells.**
* **Study of regularities and mechanisms of functional and neurochemical disorders in the central nervous system under the action of radiation with different values of linear energy transfer. Obtaining comparative data on the laws of induction of functional disorders in the brain structures under the action of rare and dense ionizing radiation used in the treatment of cancer diseases. Search and study of drugs with neuroprotective effect to the influence of ionizing radiation of different quality.**

6.   Group size, composition and budget

-List the JINR personnel involved in the project, including name, status (e.g. PI, researcher, post-doc, student, engineer, technician…) and FTE. Mention the total number of people in the collaboration.

**The total number of people in the collaboration is 31.**

**JINR personnel involved in the project:**

1. **A.V. Agapov, researcher, 1.0 FTE;**
2. **I.V. Alexandrova, engineer, 1.0 FTE;**
3. **O.V. Belov, researcher, 0.5 FTE;**
4. **K. Belokopytova, researcher, 1.0 FTE;**
5. **K.Sh. Voskanyan, leader researcher, 1.0 FTE;**
6. **V.N. Gaevsky, leader engineer, 1.0 FTE;**
7. **Ye.A. Gritskova, engineer, 1.0 FTE;**
8. **G.V. Donskaya, leader engineer, 1.0 FTE;**
9. **I.I. Klochkov, engineer, 1.0 FTE;**
10. **Ye.I. Luchin, senior researcher**
11. **I.Ye. Miller, technician,** **1.0 FTE;**
12. **G.V. Mytsin, head of division, 1.0 FTE;**
13. **A.G. Molokanov, senior researcher, 1.0 FTE;**
14. **S.A. Pisareva, engineer, 1.0 FTE;**
15. **A.V. Rzyanina, senior researcher, 1.0 FTE;**
16. **I. Khassenona, researcher, 1.0 FTE;**
17. **S.V. Shvidky, vice- head of division, 1.0 FTE;**
18. **K.N. Shipulin, researcher, 1.0 FTE.**

-Present the JINR group budget for the period of time of the requested extension, specifying the main budget items (equipment, computing, salaries, common funds, travel…)

**JINR group budget for the period 2021-2022:**

**Equipment and materials – 30 000 USD;**

**DLNP Phasotron operation – 1000 hours;**

**Traveling expenses - 30 000 USD.**

-Indicate the use or needs of JINR computing resources for the group and for the project if any.