

PHYSICS AND TECHNIQUE
OF ACCELERATORS

Vacuum Insulated Tandem Accelerator for Boron Neutron Capture Therapy and Other Applications

M. I. Bikchurina^{a, b}, T. A. Bykov^{a, b}, G. D. Verkhovod^{a, b}, I. S. Ibrahim^{b, c}, D. A. Kasatov^{a, b},
A. I. Kasatova^{a, b}, Ia. A. Kolesnikov^{a, b}, V. D. Konovalova^{a, b}, A. M. Koshkarev^{a, b}, A. S. Kuznetsov^{a, b},
G. M. Ostreinov^{a, b}, V. V. Porosev^{a, b}, S. S. Savinov^{a, b}, E. A. Sokolova^{a, b}, I. N. Sorokin^{a, b},
T. V. Sycheva^{a, b}, I. M. Shchudlo^{a, b}, and S. Yu. Taskaev^{a, b, *}

^a Budker Institute of Nuclear Physics, Siberian Branch, Russian Academy of Sciences, Novosibirsk, Russia

^b Novosibirsk State University, Novosibirsk, Russia

^c Tartous University, Tartous, Syria

*e-mail: taskaev@inp.nsk.su

Received November 18, 2022; revised December 16, 2022; accepted January 23, 2023

Abstract—A tandem electrostatic accelerator with an original design called a Vacuum Insulated Tandem Accelerator was proposed and developed at the Budker Institute of Nuclear Physics. Unlike conventional tandem accelerators, it does not use accelerating tubes—the high-voltage and intermediate electrodes are made in the form of nested cylinders and are fixed at a single feedthrough insulator. This design of the electrodes made it possible to provide a high rate of ion acceleration (up to 25 kV/cm). The accelerator is equipped with a set of diagnostic tools that provide the long-term stable production of a beam of protons or deuterons with an energy varying from 0.6 to 2.3 MeV and with a current varying from 0.1 to 10 mA. The ion beam is characterized by high monochromaticity, energy stability (0.1%), and high current stability (0.4%). The accelerator is used for in situ observations of the blistering of a metal irradiated with protons; for measuring the cross section of the reactions ${}^7\text{Li}(p, p'\gamma){}^7\text{Li}$, ${}^7\text{Li}(p, \alpha)\alpha$, and ${}^{11}\text{B}(p, \alpha)\alpha$; for developing boron neutron capture therapy for malignant tumors by using neutrons generated in the ${}^7\text{Li}(p, n){}^7\text{Li}$ reaction; for the radiation testing of promising materials using fast neutrons in the ${}^7\text{Li}(d, n)$ reaction; and for other applications. The accelerator became an integral part of the medical neutron source for boron neutron capture therapy: the first facility was put into operation in one of the first six BNCT clinics in the world in Xiamen, China; the next two facilities are being made for the National Center of Oncological Hadron Therapy in Pavia (Italy) and for the Blokhin National Medical Research Center of Oncology in Moscow. In this paper, the design of the accelerator and its features and parameters, as well as the results of studies carried out using the accelerator, are presented and discussed.

DOI: 10.1134/S1547477123040106

INTRODUCTION

Boron neutron capture therapy (BNCT) [1] is considered a promising method for treating malignant tumors, because it provides the selective destruction of tumor cells due to the accumulation of nonradioactive atomic nuclei of ${}^{10}\text{B}$ in them and their subsequent irradiation with neutrons. The absorption of neutron by boron leads to the nuclear reaction ${}^{10}\text{B}(n, \alpha){}^7\text{Li}$ with a high energy release in the cell, which results in its death. A therapeutic neutron beam that would best satisfy the BNCT requirements can be obtained in the threshold reaction ${}^7\text{Li}(p, n){}^7\text{Be}$ at a proton energy of about 2.5 MeV. Such an accelerator of charged particles and a lithium target were proposed and designed at the Budker Institute of Nuclear Physics. The accelerator neutron source is used to develop the BNCT method and other applications.

1. STRUCTURE OF THE VACUUM UNSATURATED TANDEM ACCELERATOR

The vacuum insulated tandem accelerator is a tandem-type linear electrostatic accelerator of charged particles with an original structure. The term *linear* characterizing this accelerator means that the ion beam passes once through the accelerating segments. The term *electrostatic* means that a constant electric field performs work on a particle, i.e., increases its energy. The term *tandem* means that the applied accelerating voltage of the constant current is used twice. Negative ions are accelerated by a positive potential applied to the central high-voltage electrode. Inside the central high-voltage electrode, negative ions convert to positive ions, which are accelerated again by the same potential. The key advantage of the concept of tandem acceleration is the halving of the necessary accelerating voltage, which significantly simplifies

electrostatic insulation and, thus, reduces the size of the accelerator and its cost.

The vacuum insulated tandem accelerator [2] has a specific structure in which accelerating tubes are not used, unlike conventional tandem accelerators. Instead of them, one uses nested intermediate electrodes (1) fixed at the feedthrough insulator (4), as is schematically shown in Fig. 1. The advantage of such an arrangement is the quite large distance between the ceramic parts of the feedthrough insulator and the ion beam, which enhances the high-voltage strength of the accelerating segments in the hope of obtaining large values of the current of the ion beam.

The initial aim of creating such an accelerator of charged particles is reaching the parameters satisfying the BNCT requirements. Such parameters—energy of 2.3 MeV and current of 10 mA—are reached at the accelerator in the Institute of Nuclear Physics, Siberian Branch, Russian Academy of Sciences, however, as the ultimate parameters. Despite the fact that the accelerator does not provide a long stable operation at these parameters, the main constraints are determined and ways to overcome these constraints are proposed. In the accelerators produced and being produced for the BNCT clinics, for the stable acquisition of proton beams with energy of 2.3 MeV, the gap between the intermediate electrodes is increased and preacceleration is added. To obtain stable proton beams with a current of 10 mA, the source of negative hydrogen ions designed at the Budker Institute of Nuclear Physics is replaced with the ion source produced by D-Pace (Canada).

2. APPLICATION OF THE VACUUM INSULATED TANDEM ACCELERATOR

As the main goal (achieving parameters that meet the BNCT requirements) has been attained, the accelerator has started to be used in other applications that required other values of energy and current lower than 2.3 MeV and 10 mA, respectively, albeit which are stable for a long time. Nowadays, in this accelerator, it is possible to obtain a stationary proton beam with energy varying from 0.6 to 2.2 MeV and current usually varying from 0.5 to 3 mA. The proton beam is characterized by its energy homogeneity of 0.1%, energy stability of 0.1%, and current stability of up to 0.4%. The accelerator makes it possible to obtain deuteron beams with similar parameters as well. With the use of the vacuum insulated tandem accelerator, the following important scientific results were obtained:

(1) The process of blistering on the surface of metals irradiated with protons with energy of 2 MeV is studied in situ in detail [3] and its effect on the neutron yield from the target made in the form of a thin lithium layer deposited onto the effectively cooled copper substrate is investigated [4]. It is established for the first time that radiation blistering does not limit the target

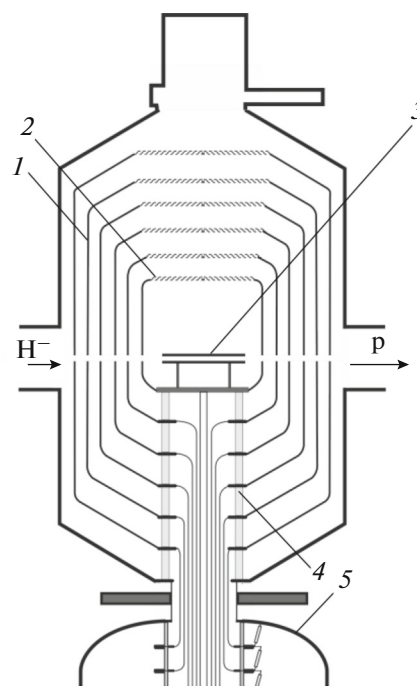


Fig. 1. Scheme of the vacuum insulated tandem accelerator: (1) intermediate electrode, (2) high-voltage electrode, (3) argon target, (4) feedthrough insulator, and (5) high-voltage source.

operation time; the processes leading to such a result is determined.

(2) It is established that neutron irradiation of the cells of human malignant glioma U251 and human glioblastoma T98G, preliminarily incubated in the medium with boron, leads to a significant suppression of their viability; irradiation of mice with a transplanted tumor leads to their recovery [5–7]; and the irradiation of large domestic animals with spontaneous tumors leads to their recovery [8].

(3) The yield of 478-keV photons from a thick lithium target and the cross section of the ${}^7\text{Li}(p,p'\gamma){}^7\text{Li}$ reaction [9], the cross section of the ${}^7\text{Li}(p,\alpha){}^4\text{He}$ reaction [10], and the neutron yield from a lithium target in the ${}^7\text{Li}(p,n){}^7\text{Be}$ reaction [11] are measured. The data are put into the databases of IBANDL and EXFOR experimental nuclear reactions.

(4) The method for measuring the sum of the dose of fast neutrons and the nitrogen dose is proposed for the first time and achieved in practice [12].

(5) The method for measuring the lithium thickness from the detection of the intensity of radiation of photons emitted in the process of inelastic scattering of a proton by a lithium nucleus was proposed and achieved for the first time [13].

(6) A compact detector of neutrons with a cast polystyrene boron-doped scintillator is developed and used for measuring the boron dose [14].

(7) By using the activation analysis method, the concentration of dangerous impurities in the speci-

mens of ceramics and steel developed for the ITER international thermonuclear reactor is measured [15].

(8) The generation of a powerful fast-neutron flux [16] is applied for the radiation testing of optical cables produced by specialists of the Saclay Nuclear Research Center for the operation of the Large Hadron Collider in CERN in the high-luminosity mode, a diamond detector of neutrons for the ITER International Thermonuclear Reactor, and neodymium magnets for a powerful linear accelerator.

(9) Thermal and epithermal neutron fluxes are used for testing new selected boron delivery drugs [17–20].

Relevant problems of the further development of the facility are increasing the current of the ion beam and expansion of the scope of its application owing to the development of methods for dosimetry, boron visualization, measurement of the cross section of the $^{11}\text{B}(p,\alpha)^4\text{He}$ reaction, obtaining cold neutron and positron fluxes, obtaining a more powerful fast-neutron flux, and other tasks.

CONCLUSIONS

A vacuum insulated tandem accelerator is proposed and designed at the Budker Institute of Nuclear Physics, it provides the long stable acquisition of proton and deuteron beams with an energy varying from 0.6 to 2.3 MeV and current varying from 0.1 to 10 mA. The ion beam is characterized by its high monochromatism and energy stability (0.1%), as well as a high current stability (0.4%). The accelerator is used for studying the dynamics of blistering on the metal surface in the process of proton implantation, measuring the cross sections of some nuclear reactions, developing the boron-neutron capture therapy of malignant tumors, the radiation testing of promising materials, and other applications.

FUNDING

This research was supported by the Russian Science Foundation, project no. 19-72-30005.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. W. Sauerwein, A. Wittig, R. Moss, and Y. Nakagawa, *Neutron and Capture Therapy: Principles and Applications* (Springer, 2012).
2. S. Taskaev et al., “Neutron source based on vacuum insulated tandem accelerator and lithium target,” *Biology* **10**, 350 (2021).
3. A. Badrutdinov et al., “In situ observations of blistering of a metal irradiated with 2-MeV protons,” *Metals* **7**, 558 (2017).
4. T. Bykov et al., “In situ study of the blistering effect of copper with a thin lithium layer on the neutron yield in the $^7\text{Li}(p,n)^7\text{Be}$ reaction,” *Nucl. Instrum. Methods Phys. Res., Sect. B* **481**, 62 (2020).
5. E. Sato et al., “Radiobiological response of U251MG, CHO-K1 and V79 cell lines to accelerator-based boron neutron capture therapy,” *J. Rad. Res.* **59**, 101 (2018).
6. E. Zavjalov et al., “Accelerator-based boron neutron capture therapy for malignant glioma: a pilot neutron irradiation study using boron phenylalanine, sodium borocaptate and liposomal borocaptate with a heterotopic U87 glioblastoma model in SCID mice,” *Int. J. Radiat. Biol.* **96**, 868 (2020).
7. V. Kanygin et al., “Dose-dependent suppression of human glioblastoma xenograft growth by accelerator-based boron neutron capture therapy with simultaneous use of two boron-containing compounds,” *Biology* **10**, 1124 (2021).
8. V. Kanygin et al., “In vivo accelerator-based boron neutron capture therapy for spontaneous tumors in large animals: case series,” *Biology* **11**, 138 (2022).
9. S. Taskaev et al., “Measurement of the $^7\text{Li}(p,p'\gamma)^7\text{Li}$ reaction cross-section and 478 keV photon yield from a thick lithium target at proton energies from 0.65 MeV to 2.225 MeV,” *Nucl. Instrum. Methods Phys. Res., Sect. B* **502**, 85 (2021).
10. S. Taskaev et al., “Cross-section measurement for the $^7\text{Li}(p,\alpha)^4\text{He}$ reaction at proton energies 0.6–2 MeV,” *Nucl. Instrum. Methods Phys. Res., Sect. B* **525**, 55 (2022).
11. M. Bikchurina et al., “The measurement of the neutron yield of the $^7\text{Li}(p,n)^7\text{Be}$ reaction in lithium targets,” *Biology* **10**, 824 (2021).
12. M. Dymova et al., “Method of measuring high-LET particles dose,” *Radiat. Res.* **196**, 192 (2021).
13. D. Kasatov et al., “Method for in situ measuring the thickness of a lithium layer,” *J. Instrum.* **15**, 10006 (2020).
14. T. Bykov et al., “Evaluation of depth-dose profiles in a water phantom at the BNCT facility at BINP,” *J. Instrum.* **16**, 10016 (2021).
15. A. Shoshin et al., “Integration of ITER diagnostic ports at the Budker Institute,” *Fusion Eng. Des.* **178**, 113114 (2022).
16. D. Kasatov et al., “Fast neutron source based on vacuum insulated tandem accelerator and lithium target,” *Prib. Tekh. Eksp.* **5**, 5 (2020).
17. K. Aiyzhy et al., “Laser Ablation of Fe_2B target enriched in ^{10}B content for boron neutron capture therapy,” *Laser Phys. Lett.* **19**, 066002 (2022).
18. A. Zaboronok et al., “Polymer-stabilized elemental boron nanoparticles for boron neutron capture therapy: initial irradiation experiments,” *Pharmaceutics* **14**, 761 (2022).
19. T. Popova et al., “Homocystamide conjugates of human serum albumin as a platform to prepare bimodal multidrug delivery systems for boron-neutron capture therapy,” *Molecules* **26**, 6537 (2021).
20. M. Vorobyeva et al., “Tumor cell-specific 2'-fluoro RNA aptamer conjugated with closododecaborate as a potential agent for boron neutron capture therapy,” *Int. J. Mol. Sci.* **22**, 7326 (2021).

Translated by E. Smirnova