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Development of a liquid Fricke dosimeter and its application together with prompt gamma-ray spectrometry for BNCT dosimetry

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Corresponding Author:	Ksenya Kuzmina Budker Institute of Nuclear Physics SB RAS RUSSIAN FEDERATION
First Author:	Ksenya Kuzmina, Bachelor's Degree
Order of Authors:	Ksenya Kuzmina, Bachelor's Degree
	Victoria Konovalova, Master's Degree
	Anna Kasatova, PhD
	Dmitry Kasatov, PhD
	Vladimir Nazmov, PhD
	Alexander Moskalensky, PhD
	Mikhail Korobeinikov, PhD
	Mikhail Petrichenkov, PhD
	Mikhail Uvarov, PhD
	Vladimir Richter, PhD
	Sergey Taskaev, PhD
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Suggested Reviewers:	

Cover letter

Dear Editor,

We have proposed and made an epithermal neutron source that is now considered to be the most attractive for Boron Neutron Capture Therapy (BNCT). The first facility has been actively used at the Budker Institute of Nuclear Physics for a decade. The second facility is installed in the hospital in Xiamen, P.R. China – there they became the second in the world to begin conducting clinical trials of the BNCT technique. We made the third facility for Blokhin National Medical Research Center of Oncology in Moscow, Russia and plan to begin clinical trials at the end of the year. We are making great efforts to develop tools and methods of dosimetry for this new treatment method, because it is very important for the treatment of patients. We believe that we have achieved significant results and therefore we are submitting this article for publication.

We believe that the publication of this article in your journal will greatly contribute to spreading the obtained results.

Sincerely yours,

Prof. Sergey Taskaev, Chief Researcher, Budker Institute of Nuclear Physics

Head of BNCT Lab., Novosibirsk State University

Highlights

1. Currently, there are no clinically applicable dosimetry methods in boron neutron capture therapy (BNCT) that account for all BNCT dose components.
2. To solve this problem, the article suggests using two methods together: a Fricke chemical dosimeter (measures the total dose) and prompt gamma-ray spectrometry (measures only the boron dose).
3. To make it sensitive to neutrons, the standard Fricke dosimeter solution was modified by adding a boron-containing substance.
4. The methods were successfully applied during an actual therapy session to treat an animal, confirming their functionality.
5. The combined use of Fricke chemical dosimetry and prompt gamma-ray spectrometry allows for the determination of the absorbed dose, which is crucial for therapy planning and outcome assessment.

Development of a liquid Fricke dosimeter and its application together with prompt gamma-ray spectrometry for BNCT dosimetry

Ksenya Kuzmina [a,b] *, Victoria Konovalova [a,b], Anna Kasatova [a,b], Dmitry Kasatov [a,b], Vladimir Nazmov [a], Alexander Moskalensky [b], Mikhail Korobeinikov [a], Mikhail Petrichenkov [a], Mikhail Uvarov [c], Vladimir Richter [a,d], Sergey Taskaev [a,b]

[a] Budker Institute of Nuclear Physics of the Siberian Branch of the Russian Academy of Sciences, 630090, Novosibirsk, Russia

[b] Novosibirsk State University, 630090, Novosibirsk, Russia

[c] Voevodsky Institute of Chemical Kinetics and Combustion of the Siberian Branch of the Russian Academy of Sciences 630090, Novosibirsk, Russia

[d] Institute of Chemical Biology and Fundamental Medicine, Siberian Division of Russian Academy of Sciences, 630090, Novosibirsk, Russia

* *kks01122002@gmail.com*

Abstract

The methodology of boron neutron capture therapy (BNCT) is actively developing worldwide and is beginning to enter clinical practice. Unlike conventional radiation therapy methods, BNCT distinguishes four components of ionizing radiation dose: boron dose, thermal neutron dose (or nitrogen dose), fast neutron dose, and gamma-ray dose. While a decade ago it was believed that the first three dose components were immeasurable (with the first two considered fundamentally unmeasurable), today there are several methods and tools available for measuring all dose components. In this study, chemical dosimetry was used to measure the total dose, specifically employing two types of ferrous sulfate liquid dosimeters: a "conventional" one and a "neutron-sensitive" variant containing sodium tetraborate. The composition of the developed dosimeters was optimized by adding xylenol orange as a complexing agent. Calibration of the dosimeter was performed using spectrophotometric methods. The developed Fricke dosimeter, combined with prompt gamma-ray spectrometry, was applied during the treatment of a domestic cat with a spontaneous tumor. This approach enabled the determination of absorbed dose in both the tumor and healthy tissue. Data obtained from these two independent dose measurement methods showed good agreement, leading to the conclusion that their combined use is advisable for BNCT treatment planning and outcome assessment.

Keywords: boron neutron capture therapy, dosimetry, Fricke dosimeter, spectrophotometry, prompt gamma-ray spectrometry

1. Introduction

Boron Neutron Capture Therapy (BNCT) is a promising approach for treating malignant tumors, based on the selective destruction of tumor cells through the accumulation of stable isotope ^{10}B followed by irradiation with epithermal neutrons. The absorption of a neutron by boron triggers the nuclear reaction $^{10}B(n,\alpha)^{7}Li$, releasing a large amount of energy precisely within the boron-containing cell, leading to its destruction [Sauerwein et al., 2012]. Clinical trials of this method using accelerator-based neutron sources have demonstrated positive outcomes [Hirose et al., 2021; Kawabata et al., 2021].

To date, there are no clinically established dosimetry methods capable of accounting for all dose components in BNCT:

- boron dose (primary dose) from the $^{10}B(n,\alpha)^{7}Li$ reaction (α-particles and ^{7}Li nuclei);
- nitrogen dose (thermal neutron dose) from the $^{14}N(n,p)^{14}C$ reaction products;
- fast neutron dose, comprising contributions from:
- epithermal and fast neutrons via elastic and inelastic scattering (primarily on hydrogen nuclei);
- gamma dose, including photon emission from neutron capture by boron ($^{10}B(n,\gamma)^{7}Li$) and hydrogen ($^{1}H(n,\gamma)^{2}D$) nuclei [International Atomic Energy Agency, 2023].

However, it is important to note that in the book [Sauerwein et al., 2012], it is stated that "the first two dose components cannot be measured in principle, but only calculated." Over the past decade, significant progress has been made in the development of dosimetry tools and methods. In particular, at the accelerator-based neutron source VITA [Taskaev et al., 2021] the following approaches are used for dosimetry during scientific research:

- activation foil sets;
- a compact detector based on a pair of cast polystyrene scintillators, one of which is boron-enriched [Bykov et al., 2021];
- a developed activation monitor for epithermal neutron flux measurement [Byambatseren et al., 2025];
- a proposed and implemented "cellular dosimeter" [Dymova et al., 2021];
- prompt gamma-ray spectroscopy method [Bikchurina et al., 2023].

The prompt gamma-ray spectroscopy method [Kobayashi and Kanda, 1983] enables real-time monitoring of boron accumulation in malignant tumor tissue and quantifies the boron dose contribution to the total radiation dose. The technique relies on detecting the prompt gamma-ray (478 keV) emitted when the ^{7}Li nucleus (produced in the $^{10}B(n,\alpha)^{7}Li$ reaction) transitions from its first excited state ($^{7}Li^{*}$, 478 keV) to the ground state. Due to the extremely short decay time (~10^{-13} sec), the detected gamma line appears as a broadened peak at 478 keV in the spectrum. With sufficient detector energy resolution, this peak can be clearly distinguished from background radiation. The boron dose is calculated based on the count rate of 478 keV events, which is proportional to the ^{10}B concentration and thermal neutron flux.

Italian researchers [Colombo et al., 2024] have highlighted the need for advancing dosimetric methods in BNCT, conducting measurements at the TRIGA Mark II research reactor of the University of Pavia. Their work demonstrated the feasibility of prompt gamma-ray spectrometry for BNCT applications, employing a $LaBr_3$(Ce+Sr) scintillation detector for photon detection. Studies on CdTe double-sided strip detectors for prompt gamma-ray spectrometry in BNCT are presented in [Chiu et al., 2025].

Several works address modeling of prompt gamma-ray spectrometry. The BNCT-SPECT system developed in [Isao Murata et al., 2021] enables Monte Carlo (MCNP5) calculations of boron dose during

BNCT, proposing a GAGG scintillator detector with claimed 5% calculation accuracy. For comprehensive dose assessment, this work advocates chemical dosimetry.

An effective chemical dosimetric system for BNCT must meet specific requirements:

- high radiation-chemical yield independent of radiation type and variable conditions (reagent concentration, temperature, pH, dissolved gases);
- pre- and post-irradiation stability;
- compatibility with standard purity reagents.

The ferrous sulfate (Fricke) dosimeter best fulfills these criteria [Zakaria et al., 2021]. Its operation principle, detailed in [Schreiner, 2004], involves water radiolysis-induced oxidation of Fe^{2+} to Fe^{3+} via free radical reactions. Sensitivity enhancement through xylenol orange addition enables spectrophotometric Fe^{3+} detection and visual dose assessment. [Scotti et al., 2022] optimized concentrations to 1.00-0.40 mM ferrous ammonium sulfate and 0.200-0.166 mM xylenol orange for 0-42 Gy dose range.

[Gambarini et al., 2017] characterized optical absorption spectra (300-800 nm) of xylenol orange-based Fricke gel dosimeters, finding spectral variations primarily dependent on dye type rather than gelling agents (agarose/gelatin). Their earlier work [Gambarini et al., 2002] employed boron-loaded Fricke gels at the TAPIRO reactor to isolate $^{10}B(n,\alpha)$ contributions by subtracting $^{14}N(n,p)$ background. [Saeedi-Sini et al., 2024] confirmed linear response (0.05-5 accelerator gelatin/polyvinyl alcohol matrix effects.

This study aims to develop a ferrous sulfate dosimetric system for BNCT.

The results obtained by chemical dosimetry are presented in comparison with prompt gamma-ray spectrometry measurements.

2. Experimental details

2.1. Development of a dosimeter

For the experiment, following literature data, we prepared four Fricke dosimeter samples, two of which contained boric acid to achieve a ^{10}B concentration of 40 ppm in the solution. After preparation, the samples were irradiated using the accelerator-based neutron source VITA. Figure 1 shows the optical absorption spectra of the dosimeters measured with a Varian Cary-50 UV spectrophotometer. The experiment used four Fricke dosimeter samples: an unirradiated sample with 0 ppm ^{10}B, an unirradiated sample with 40 ppm ^{10}B, a sample irradiated with 0.8 Gy dose containing 0 ppm ^{10}B, and a sample irradiated with 8 Gy dose containing 40 ppm ^{10}B. The absorbed dose was estimated through Monte Carlo numerical modeling of neutron and gamma radiation transport. The spectra show insufficient differences to be used for quantitative determination of absorbed ionizing radiation dose.

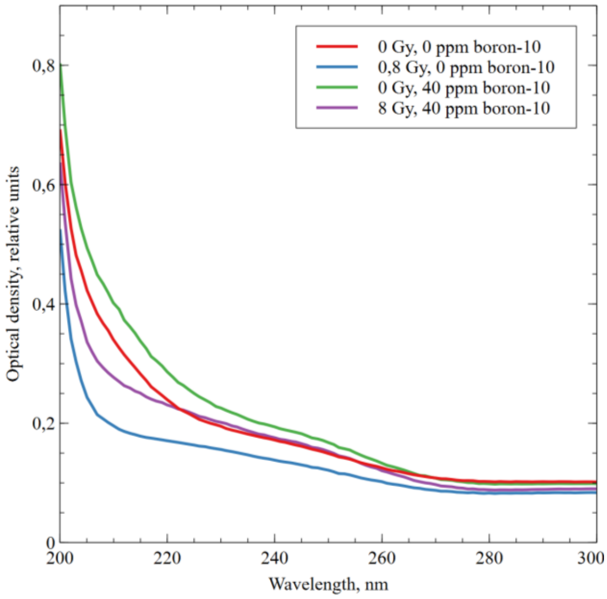

Fig. 1. Absorption spectrum of dosimeters

To increase the dosimeter's sensitivity to radiation dose, xylenol orange was added as a complexing agent, serving as a metallochromic indicator for direct complexometric determination of Fe^{3+} ions. This modification enhances Fe^{3+} detection sensitivity and enables visual dose assessment through color changes in the visible spectrum. Boric acid was replaced with sodium borate (sodium tetraborate) following the protocol [Gambarini et al., 2017].

The "conventional" Fricke dosimeter was prepared by adding to 1 liter of water: 0.4 g ammonium iron(II) sulfate, 5.5 ml concentrated sulfuric acid, and 0.13 g xylenol orange. For the "neutron-sensitive" Fricke dosimeter, 1.8 g sodium tetraborate was additionally included to achieve 40 ppm ^{10}B concentration in the final solution. The solutions were thoroughly mixed using a magnetic stirrer for 20 minutes at room temperature, resulting in clear solutions without precipitate.

2.2. Composition Testing

Composition testing using the Shimadzu ICPE-9800 spectrometer revealed that the "conventional" sample contained 27 µg/L iron with no detectable boron, while the "neutron-sensitive" sample contained 28 µg/L iron and 26 µg/L boron.

For visual demonstration of the color change caused by Fe^{3+}-xylenol orange complex formation, samples were irradiated with electron beams up to 1000 Gy at the BINP SB RAS Radiation Technology Center using the PLA-10 accelerator. The irradiated samples are shown in Figure 2.

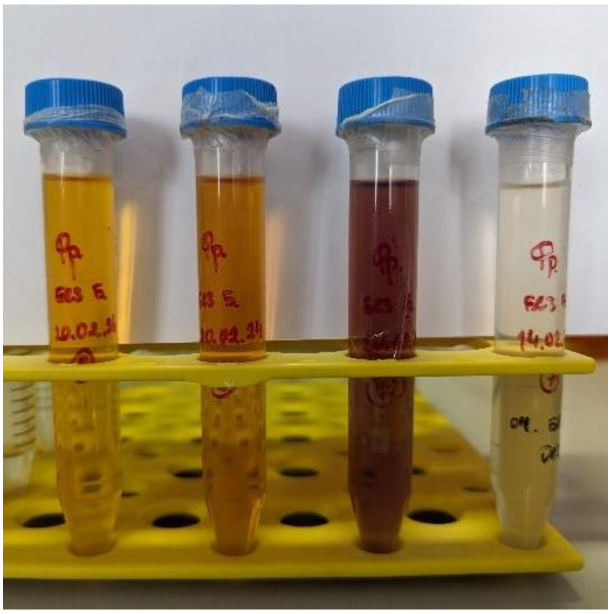

Fig. 2. Irradiated "conventional" Fricke dosimeters: Dose increases from left to right (far left – unirradiated, far right – 1000 Gy)

2.3. Calibration of Dosimeters

To construct the calibration curve, prepared samples were irradiated using a ^{137}Cs photon source by placing them at varying distances from the radiation source for 24-hour exposures. The sample set consisted of 4 "conventional" and 4 "neutron-sensitive" dosimeters, which received different doses: 0 Gy (control), 1 Gy, 2 Gy, and 8 Gy. To achieve a 1 Gy dose, samples were irradiated for 24 hours at 13.1 cm from the source; 2 Gy was delivered at 9.3 cm, and 8 Gy at 4.6 cm. The sample arrangement is shown in Figure 3.

Fig. 3. Photo of dosimeter placement for calibration using a ^{137}Cs source

The samples were analyzed using a Shimadzu UV-3600 Plus spectrophotometer after irradiation. Figure 4 shows the sample placement in the spectrophotometer.

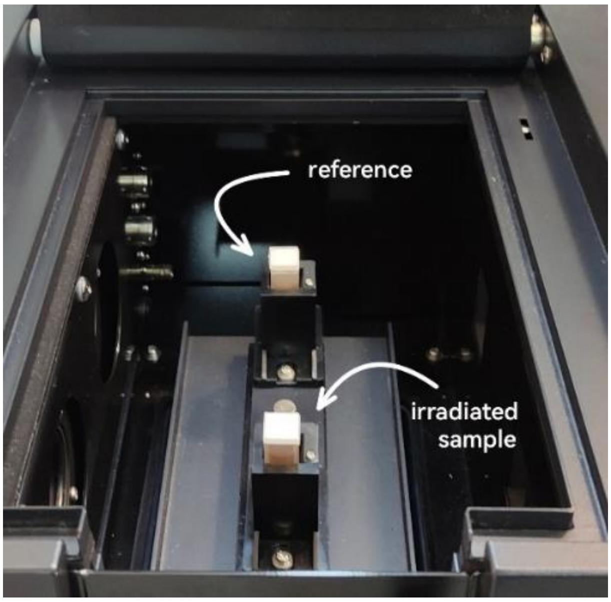

Fig. 4. Arrangement of cuvettes in the Shimadzu UV-3600 Plus spectrophotometer (reference – unirradiated sample)

The absorption spectra of the studied samples are shown in Figure 5. Since the optical design of this spectrophotometer allows comparative measurements of irradiated samples against a control, the obtained spectra were displayed already normalized to the non-irradiated sample. The spectra clearly show two peaks: at 440 nm and at 540 nm. The latter peak indicates the formation of an Fe^{3+} complex with xylenol orange.

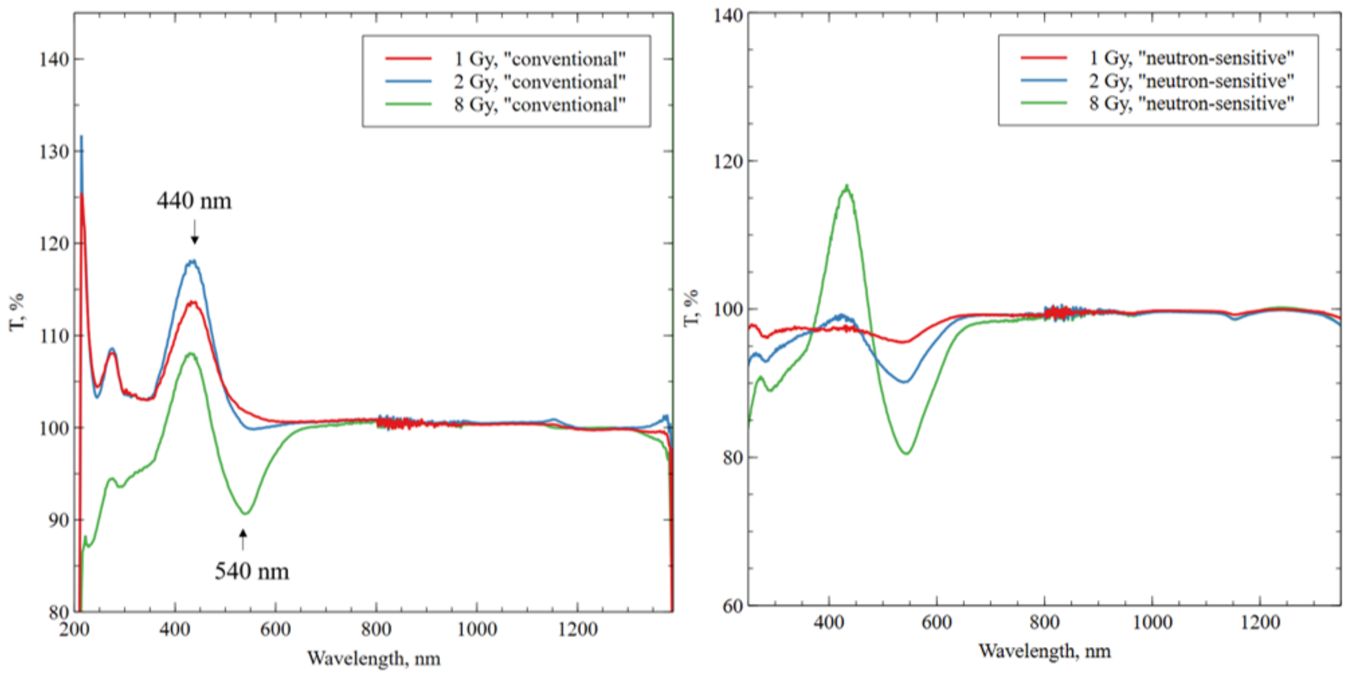

Fig. 5. Absorption spectra of irradiated "conventional" and "neutron-sensitive" Fricke dosimeters

Initially, it was hypothesized that the 440 nm peak might be associated with solution fluorescence, since xylenol orange exhibits its fluorescence maximum at 440 nm excitation wavelength. However, this hypothesis was refuted following fluorescence spectroscopy measurements conducted on a Shimadzu RF-6000 spectrofluorophotometer. Figure 6 presents the fluorescence spectra obtained under 440 nm excitation. The data demonstrate negligible differences between the spectra of different samples.

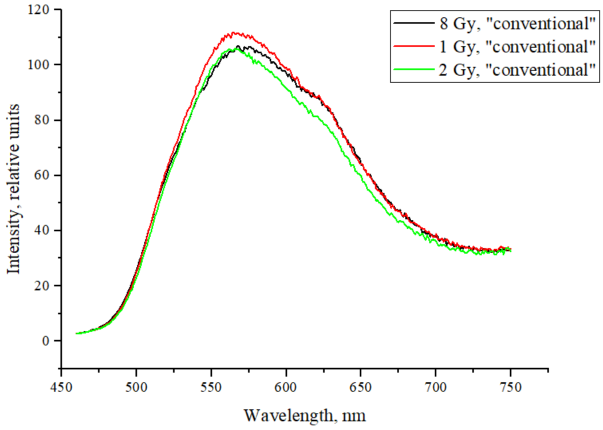

Fig. 6. Fluorescence spectra of dosimeters excited at 440 nm

The spectra shown in Figure 5 were fitted with a sum of Gaussian distributions (Figure 7). The peak at 540 nm, corresponding to absorption, was of primary interest. The only statistically significant difference between samples was observed in the coefficient B preceding the exponential term, which served as the basis for calibration (Figure 8):

$$y = A \cdot \exp\left(-\frac{(x - x_1)^2}{\sigma_1^2}\right) - B \cdot \exp\left(-\frac{(x - x_2)^2}{\sigma_2^2}\right) \quad (1)$$

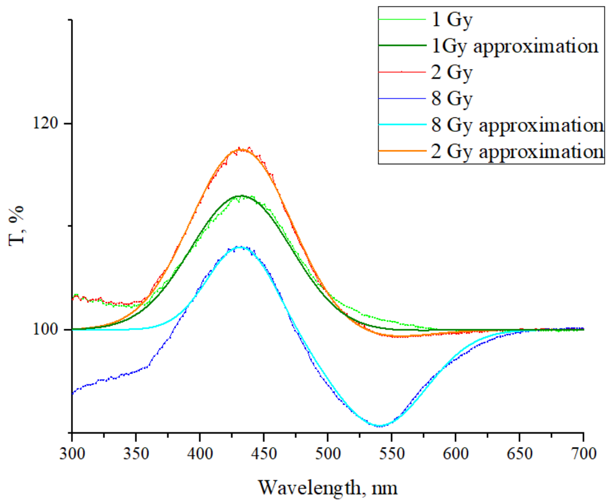

Fig. 7. Approximation of the obtained absorption spectra of "conventional" dosimeters

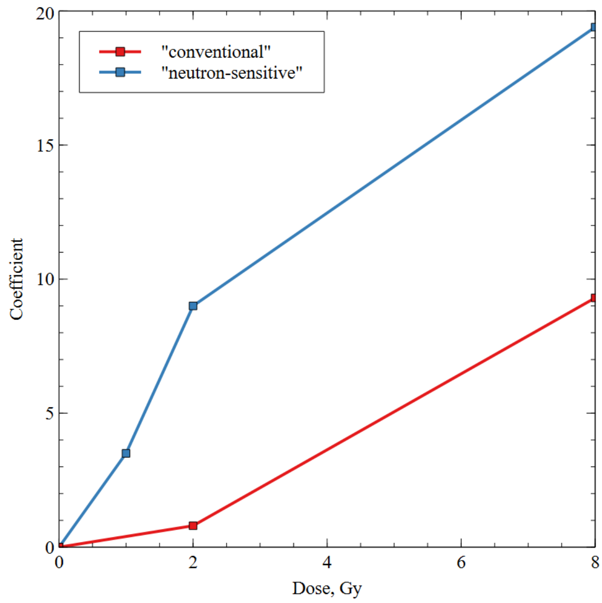

Fig. 8. Calibration of dosimeters using a ^{137}Cs source

4. Discussion and conclusion

The developed "neutron-sensitive" Fricke dosimeter was applied during boron neutron capture therapy for a domestic cat with a spontaneous tumor. The irradiation was performed using the accelerator-based neutron source VITA. The Fricke dosimeter was placed on the surface of the beam shaping assembly [Taskaev, 2019].

After the cat's treatment, the irradiated Fricke dosimeter solution was analyzed using a Shimadzu UV-3600 Plus spectrophotometer. The spectrum of the irradiated dosimeter, compared to calibration spectra, is shown in Fig. 9. By performing linear approximation, the total equivalent dose was determined to be 35 ± 6 Gy-eq. Although this exceeds the calibrated range, linearity is assumed to hold up to 100 Gy [De Dios et al., 2017].

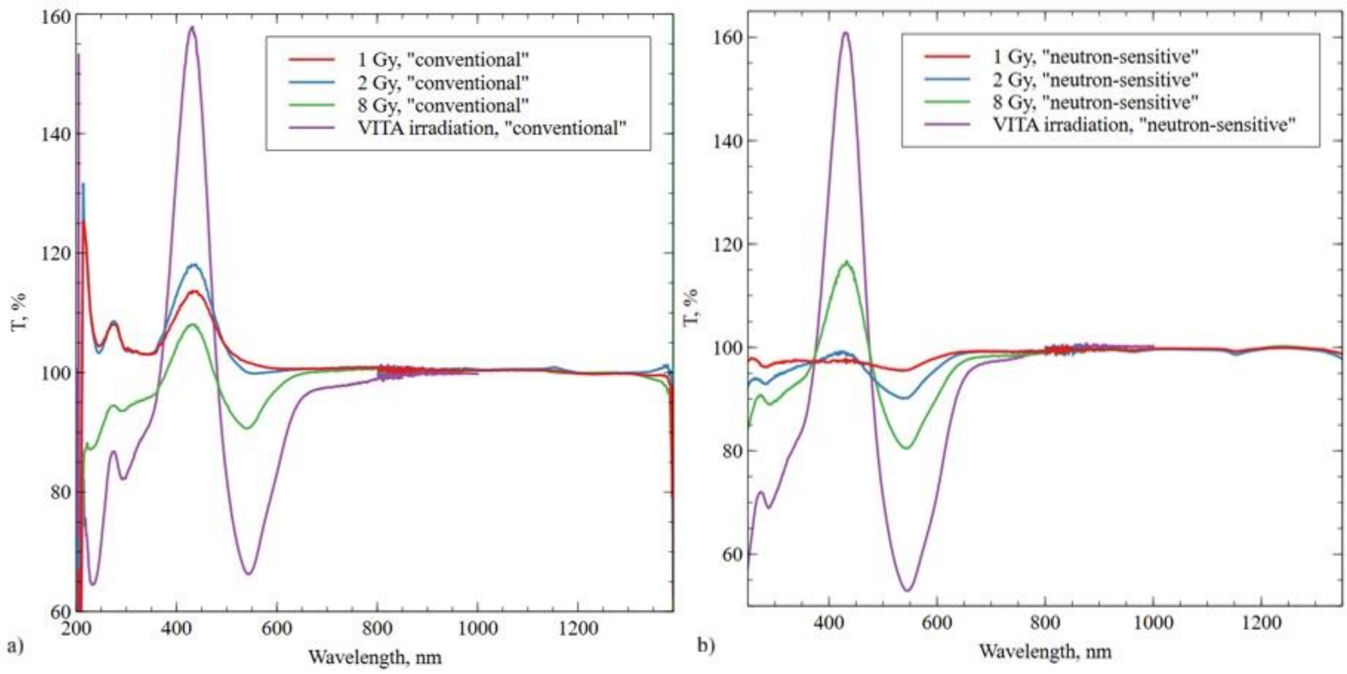

Fig 9. Absorption spectra of dosimeters irradiated at the VITA accelerator compared with ^{137}Cs-irradiated samples: a) "conventional" dosimeter, b) "neutron-sensitive" dosimeter

In the study by [Sycheva et al., 2023], numerical simulation of neutron and gamma-ray transport was used to calculate the spatial distribution of all four dose components considered in boron neutron capture therapy (BNCT): boron dose, nitrogen dose, fast neutron dose, and gamma-ray dose. The same work demonstrated that the results of spatial measurements of boron dose and gamma dose, obtained using a compact detector with paired lithium-loaded polystyrene scintillators (one of which was enriched with boron), agree well with the calculated data [Bykov et al., 2021].

The calculations revealed that, under the treatment conditions for the cat, the ratio of the therapeutic dose (boron dose) to the sum of all other doses (nitrogen dose, fast neutron dose, and gamma dose) was 4.3 at a boron concentration of 40 ppm. Since the boron concentration in the Fricke "neutron-sensitive" dosimeter was 26 ppm, and the boron dose is proportional to boron concentration, the ratio of boron dose to the sum of the remaining doses contributing to the Fricke dosimeter reading was 2.8. Thus, out of the total Fricke dosimeter dose of 35 ± 6 Gy-eq, the presence of boron at 26 ppm contributed 26 ± 4 Gy-eq, while the remaining 9 ± 2 Gy-eq came from the other three dose components. Given that the dosimeter was placed on the surface, the measured sum of the three dose components was maximal, as supported by the data in [Sycheva et al., 2023].

Therefore, the results indicate that the maximum equivalent dose received by cells without boron was 9 ± 2 Gy-eq. Taking into account the relative biological effectiveness (RBE) of fast neutrons (3.2), thermal neutrons (3), and photons (1), the total physical dose was determined to be 6.5 ± 1.5 Gy.

To estimate the boron dose, it was necessary to determine the boron concentration in the tumor and healthy tissues. This information was obtained using prompt gamma-ray spectrometry, where the energy spectrum of photons emitted from the irradiated cat was measured with an HPGe gamma-ray spectrometer. The experimental setup is shown in Fig. 10. The spectrometer was placed in an adjacent bunker, observing the irradiated object through a hole in the concrete wall. Neutron shielding (acrylic glass and cadmium) was used to protect the spectrometer's detector from neutron interference.

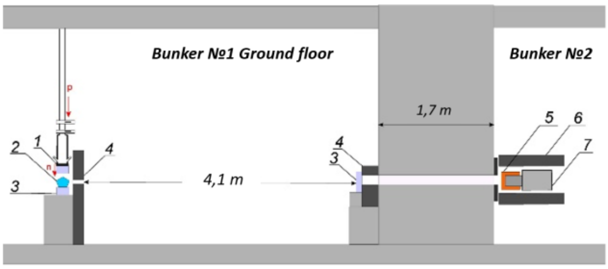

Fig. 10. Experimental setup for boron dose measurement using prompt gamma-ray spectrometry: 1 – lithium target, 2 – animal, 3 – plexiglas, 4 – lead shielding, 5 – cadmium layer, 6 – lead collimator, 7 – gamma-ray spectrometer

The characteristic energy spectrum of photons measured by the spectrometer is shown in Fig. 11. The spectrum clearly displays a Doppler-broadened 478 keV line, reflecting the number of $^{10}B(n,\alpha)^{7}Li$ reactions within the detector's field of view. A lead collimator (2.5 cm wide and 5 cm high) was placed in front of the irradiated object (the cat). Given that the width of the cat's head in the observation area was 5 cm, the detection volume was estimated to be 62.5 cm^3. The cat was positioned such that the entire tumor (volume 17 cm^3) fell within the detection region, while the volume of healthy tissue in the detection area was taken as 45.5 cm^3 in subsequent calculations.

Two key observations can be made from Fig. 11. The intensity of the 568 keV line, resulting from the $^{113}Cd(n,\gamma)^{114}Cd$ reaction, remains the same at the beginning and end of irradiation. This indicates stability in the neutron flux. Additionally, the constant intensity of the 517 keV line (from the $^{35}Cl(n,\gamma)^{36}Cl$ reaction) confirms the stability of the neutron flux and reflects the volume of living tissue within the detection region. The intensity of the 478 keV line (due to the neutron capture reaction in boron) is nearly twice as low at the end of irradiation compared to the beginning. This is attributed to the gradual decrease in boron concentration in the cells over time.

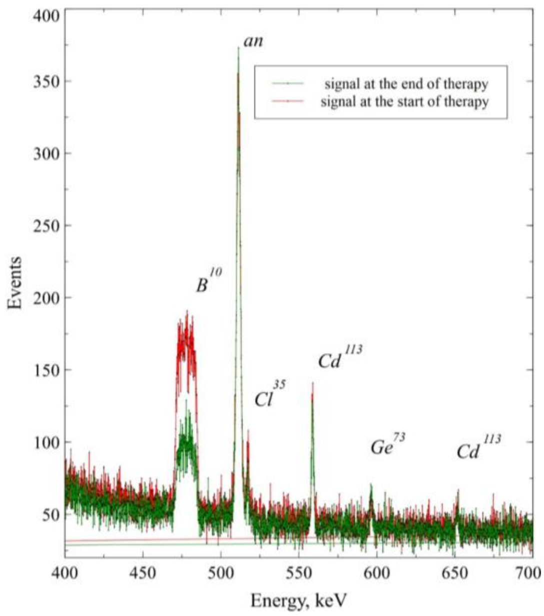

Fig 11. Gamma-ray spectrum obtained during BNCT of a laboratory animal

During the irradiation period of the cat, the energy spectrum of photons from the detection region was measured in 22 time intervals. Over the entire observation period, $1.73 \cdot 10^6$ photons with an energy of 478 keV were registered, resulting from the $^{10}B(n,\alpha)^7Li$ reaction. Taking into account the detector sensitivity (located at a distance of 610 cm) of $1.3 \cdot 10^{-6}$ [Bikchurina et al., 2021] and the probability of photon emission in the reaction (93.9%), we determined that $1.4 \cdot 10^{12}$ $^{10}B(n,\alpha)^7Li$ reactions occurred in the detection volume during irradiation. Since each reaction releases an average of 2.34 MeV (shared between the α-particle and the lithium nucleus), we calculated that 0.53 J of energy was deposited in the detection volume of 62.5 cm^3. The accuracy of the energy determination is influenced by multiple processes and is estimated to be within 10%.

When using boronophenylalanine (BPA), it is commonly assumed that the boron concentration in tumor cells is three times higher than in healthy tissue [International Atomic Energy Agency, 2023]. Based on this ratio, we determined that a tumor volume of 17 cm^3 received a boron dose of 16.4 ± 1.6 Gy, while healthy tissue with a volume of 45.5 cm^3 received a boron dose of 5.5 ± 0.6 Gy. The boron concentration in the tumor was 17.8 ppm, and in healthy tissue, it was 5.9 ppm.

Including the sum of the other three dose components, measured by the Fricke dosimeter (6.5 ± 1.5 Gy), we concluded that the tumor in the irradiated cat received a total ionizing radiation dose of 23 ± 3 Gy, while the dose absorbed by the surrounding healthy tissue did not exceed 12 ± 2 Gy.

Thus, the combined use of Fricke chemical dosimetry and prompt gamma-ray spectrometry allows for the determination of the absorbed dose, which is crucial for therapy planning and outcome assessment.

CRediT authorship contribution statement

Ksenya Kuzmina: Data curation, Formal analysis, Investigation, Visualization, Roles/Writing - original draft. **Victoria Konovalova:** Data curation, Formal analysis, Investigation, Visualization, Roles/Writing - original draft. **Anna Kasatova:** Data curation, Formal analysis, Investigation, Methodology, Supervision, Roles/Writing - original draft. **Dmitry Kasatov:** Conceptualization, Data curation, Methodology, Supervision, Validation, Writing - review & editing. **Vladimir Nazmov:** Investigation, Methodology, Software, Visualization. **Alexander Moskalensky:** Investigation, Methodology, Software, Visualization. **Mikhail Korobeinikov:** Investigation, Resources, Software, Visualization. **Mikhail Petrichenkov:** Investigation, Software, Visualization. **Mikhail Uvarov:** Investigation, Methodology, Software, Visualization. **Vladimir Richter:** Methodology, Supervision, Writing - review & editing. **Sergey Taskaev:** Conceptualization, Funding acquisition, Project administration, Resources, Validation, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

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Institutional Review Board Statement

The animal study was carried out according to the principles of humanity and the European Community Directive (86/609/EEC) and was approved by the Ethical Committee of Institute of Cytology and Genetics SB RAS, Novosibirsk, Russian Federation (protocol code 91, "Boron neutron capture therapy in domestic cats and dogs", date of approval 5.10.2021).

References

Bikchurina M., Bykov T., Kasatov D., Kolesnikov Ia., Makarov A., Shchudlo I., Sokolova E., Taskaev S., 2021. *The measurement of the neutron yield of the $^{7}Li(p,n)^{7}Be$ reaction in lithium targets.* Biology 10, 824. doi:10.3390/biology10090824.

Bikchurina M., Bykov T., Ibrahim I., Kasatova A., Kasatov D., Kolesnikov Ia., Konovalova V., Kormushakov T., Koshkarev A., Kuznetsov A., Porosev V., Savinov S., Shchudlo I., Singatulina N., Sokolova E., Sycheva T., Taskaeva I., Verkhovod G., Taskaev S., 2023. *Dosimetry for Boron Neutron Capture Therapy Developed and Verified at the Accelerator-based Neutron Source VITA.* Front. Nucl. Eng. 2, 1266562. doi:10.3389/fnuen.2023.1266562.

Byambatseren E., Bykov T., Kasatov D., Kolesnikov Ia., Savinov S., Shein T., Taskaev S., 2025. *Study of the influence of moderator material on sensitivity of the epithermal neutron flux detector using the $^{71}Ga(n,\gamma)^{72}Ga$ reaction.* Applied Radiation and Isotopes 222, 111844. doi:10.1016/j.apradiso.2025.111844.

Bykov, T., Kasatov, D., Koshkarev, A., Makarov, A., Porosev, V., Savinov, G., Shchudlo, I., Taskaev, S., Verkhovod, G., 2021. *Initial trials of a dose monitoring detector for boron neutron capture therapy.* JINST, vol. 16, P01024. doi:10.1088/1748-0221/16/01/P01024.

Chiu, I.-H., Osawa, T., Sumita, T., Ikeda, M., Ninomiya, K., Takeda, S., Minami, T., Takahashi, T., Watanabe, S., 2025. *Development of a real-time boron imaging method for BNCT using CdTe-DSD at the JRR-3.* Applied Radiation and Isotopes 222, 111845. doi:10.1016/j.apradiso.2025.111845.

Colombo G., Caracciolo A., Introini M., Borghi G., Carminati M., Protti N., Altieri S., Agosteo S., Fiorini C., 2024. *Study of the thermal neutron activation of a gamma-ray detector for BNCT dose monitoring.* Journal of Instrumentation, Vol. 19, No. 05, p. P05047. doi: 10.1088/1748-0221/19/05/P05047.

De Dios L.J., Giménez A., Cespón C., 2017. *A new method for dosimetry standardization using ^{137}Cs biological irradiator based on Fricke solution*. Sensors and Actuators B: Chemical, Volume 253, 784-793. doi:10.1016/j.snb.2017.06.164.

Dymova, M., Dmitrieva, M., Kuligina, E., Richter, V., Savinov, S., Shchudlo, I., Sycheva, T., Taskaeva, I., & Taskaev, S., 2021. *Method of Measuring High-LET Particles Dose.* Radiation Research 196(2), 192-196. doi:10.1667/RADE-21-00015.1.

Gambarini G., Birattari C., Colombi C., Pirola L., Rosi G., 2002. *Fricke gel dosimetry in boron neutron capture therapy.* Radiat. Prot. Dosim. 101(1-4), 419-422. doi:10.1093/oxfordjournals.rpd.a006015.

Gambarini G., Veronese I., Bettinelli L., Felisi M., Gargano M., Ludwig N., Lenardi C., Carrara M., Collura G., Gallo S., Longo A., Marrale M., Tranchina L., d'Errico F., 2017. *Study of optical absorbance and MR relaxation of Fricke xylenol orange gel dosimeters.* Radiat. Meas. 106, 622-627. doi:10.1016/j.radmeas.2017.03.024.

Hirose K., Konno A., Hiratsuka J., Yoshimoto S., Kato T., Ono K., Otsuki N., Hatazawa J., Tanaka H., Takayama K., Wada H., Suzuki M., Sato M., Yamaguchi H., Seto I., Ueki Y., Iketani S., Imai S., Nakamura T., Ono T., Endo H., Azami Y., Kikuchi Y., Murakami M., Takai Y., 2021. *Boron neutron capture therapy using cyclotron-based epithermal neutron source and borofalan (^{10}B) for recurrent or locally advanced head and neck cancer (JHN002): An open-label phase II trial.* Radiother Oncol. 155, 182-187. doi:10.1016/j.radonc.2020.11.001.

International Atomic Energy Agency, 2023. *Advances in Boron Neutron Capture Therapy*. Vienna.

Kawabata S., Suzuki M., Hirose K., Tanaka H., Kato T., Goto H., Narita Y., Miyatake S.I., 2021. *Accelerator-based BNCT for patients with recurrent glioblastoma: a multicenter phase II study*, Neurooncol Adv. 3(1), vdab067. doi: 10.1093/noajnl/vdab067.

Kobayashi T., and Kanda K., 1983. *Microanalysis system of ppm-order ^{10}B concentrations in tissue for neutron capture therapy by prompt gamma-ray spectrometry.* Nucl. Instrum. Methods Phys. Res. 204, 525–531. doi:10.1016/0167-5087(83)90082-0.

Murata I., Kusaka S., Minami K., Saraue N., Tamaki S., Kato I., Sato F., 2021. *Design of SPECT for BNCT to measure local boron dose with GAGG scintillator.* Applied Radiation and Isotopes 181, 110056. doi:10.1016/j.apradiso.2021.110056.

Saeedi-Sini, S. A., Sina, S., Sadeghi, M.H., & Farajzadeh, E., 2024. *Development and characterization of a Fricke gel dosimeter for precise measurement in low-dose photon fields.* JINST 19, P06019. doi:10.1088/1748-0221/19/06/P06019.

Sauerwein W.A.G., Wittig A., Moss R., Nakagawa Y., 2012. *Neutron Capture Therapy: Principles and Applications.* Heidelberg Springer Verlag, Berlin.

Scotti, M., Arosio, P., Brambilla, E., Gallo, S., Lenardi, C., Locarno, S., Orsini, F., Pignoli, E., Pedicone, L., Veronese, I., 2022. *How Xylenol Orange and Ferrous Ammonium Sulphate Influence the Dosimetric Properties of PVA-GTA Fricke Gel Dosimeters: A Spectrophotometric Study.* Gels 8, 204. doi:10.3390/gels8040204.

Schreiner L. J. *Review of Fricke gel dosimeters*, 2004. J. Phys.: Conf. Ser. 3, 9. doi:10.1088/1742-6596/3/1/003.

Sycheva T.V., Berendeev E.A., Verkhovod G.D., Taskaev S.Yu, 2023. *A Neutron Beam Shaping Assembly for Boron Neutron Capture Therapy of Superficial Tumors.* SIBERIAN JOURNAL OF PHYSICS 18(3), 31-42. (In Russ.) doi:10.25205/2541-9447-2023-18-3-31-42.

Taskaev S., 2019. *Development of an Accelerator-Based Epithermal Neutron Source for Boron Neutron Capture Therapy.* Physics of Particles and Nuclei, Vol. 50, No. 5, pp. 569–575. doi:10.1134/S1063779619050228.

Taskaev S., Berendeev E., Bikchurina M., Bykov T., Kasatov D., Kolesnikov I., Koshkarev A., Makarov A., Ostreinov G., Porosev V., Savinov S., Shchudlo I., Sokolova E., Sorokin I., Sycheva T., Verkhovod G., 2021. *Neutron Source Based on Vacuum Insulated Tandem Accelerator and Lithium Target.* Biology 10, 350. doi:10.3390/biology10050350

Zakaria A., Lertnaisat P., Islam M., Meesungnoen J., Katsumura Y., Jay-Gerin J.-P., 2021. *Yield of the Fricke dosimeter irradiated with the recoil α and Li ions of the* $^{10}B(n, \alpha)^{7}Li$ *nuclear reaction: effects of multiple ionization and temperature.* Canadian Journal of Chemistry 99(4), 425-435. doi:10.1139/cjc-2020-0381.

Figure 1

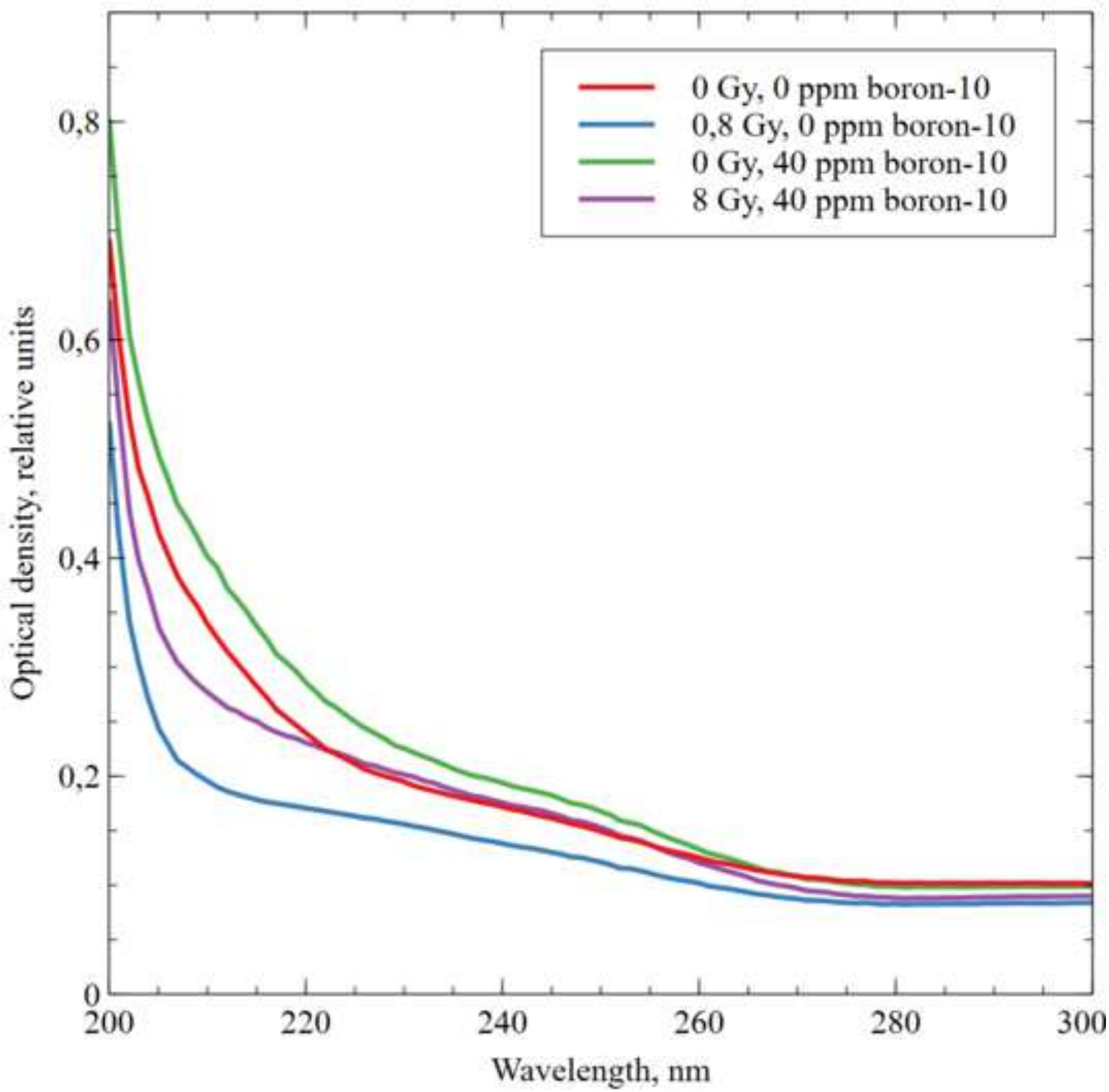
0 Gy, 0 ppm boron-10
0,8 Gy, 0 ppm boron-10
0 Gy, 40 ppm boron-10
8 Gy, 40 ppm boron-10
Optical density, relative units
0
0,2
0,4
0,6
0,8
200
220
240
260
280
300
Wavelength, nm

Figure 8

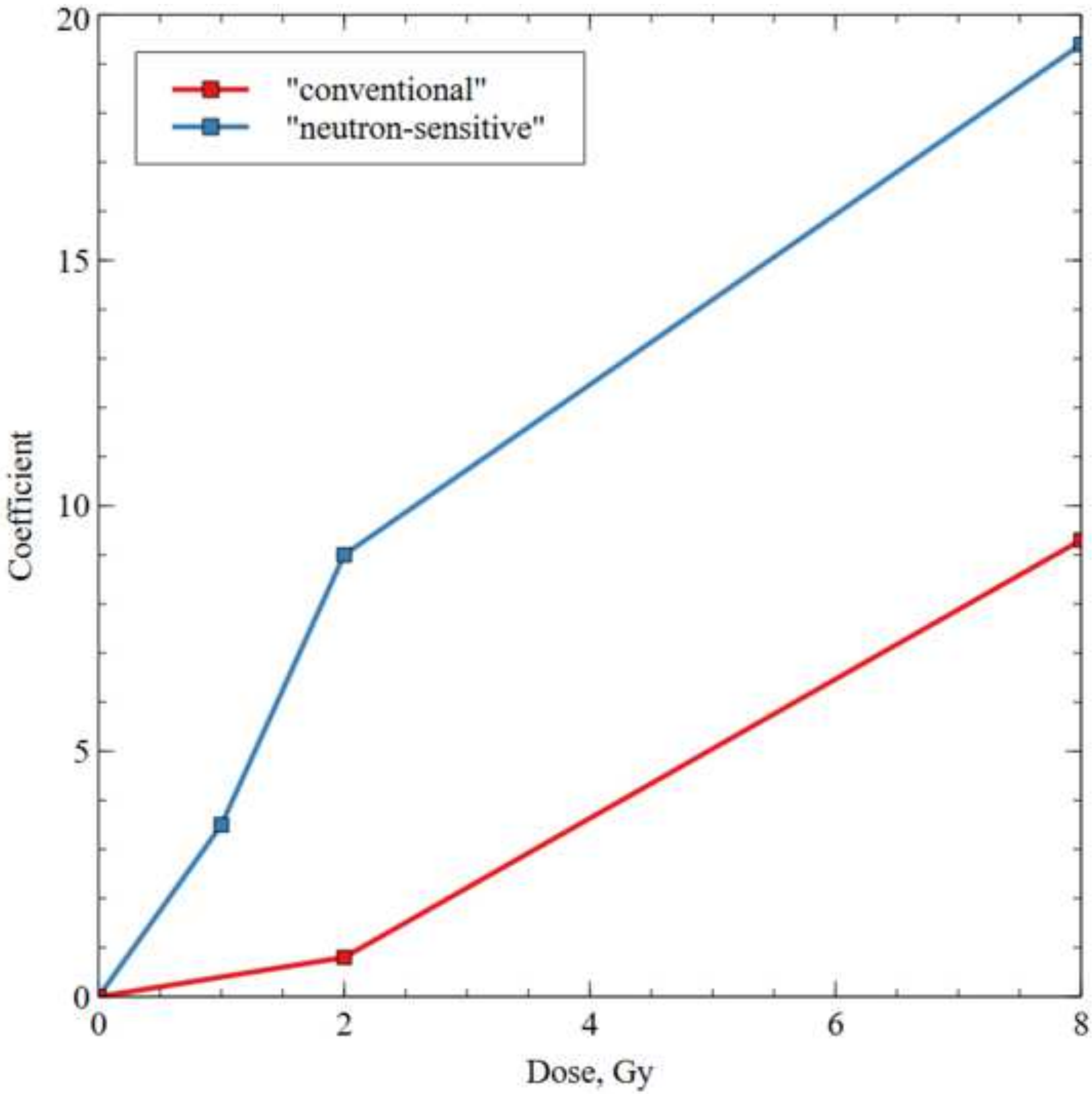
20
15
10
5
0
0
2
4
6
8
Coefficient
Dose, Gy
"conventional"
"neutron-sensitive"

Figure 2

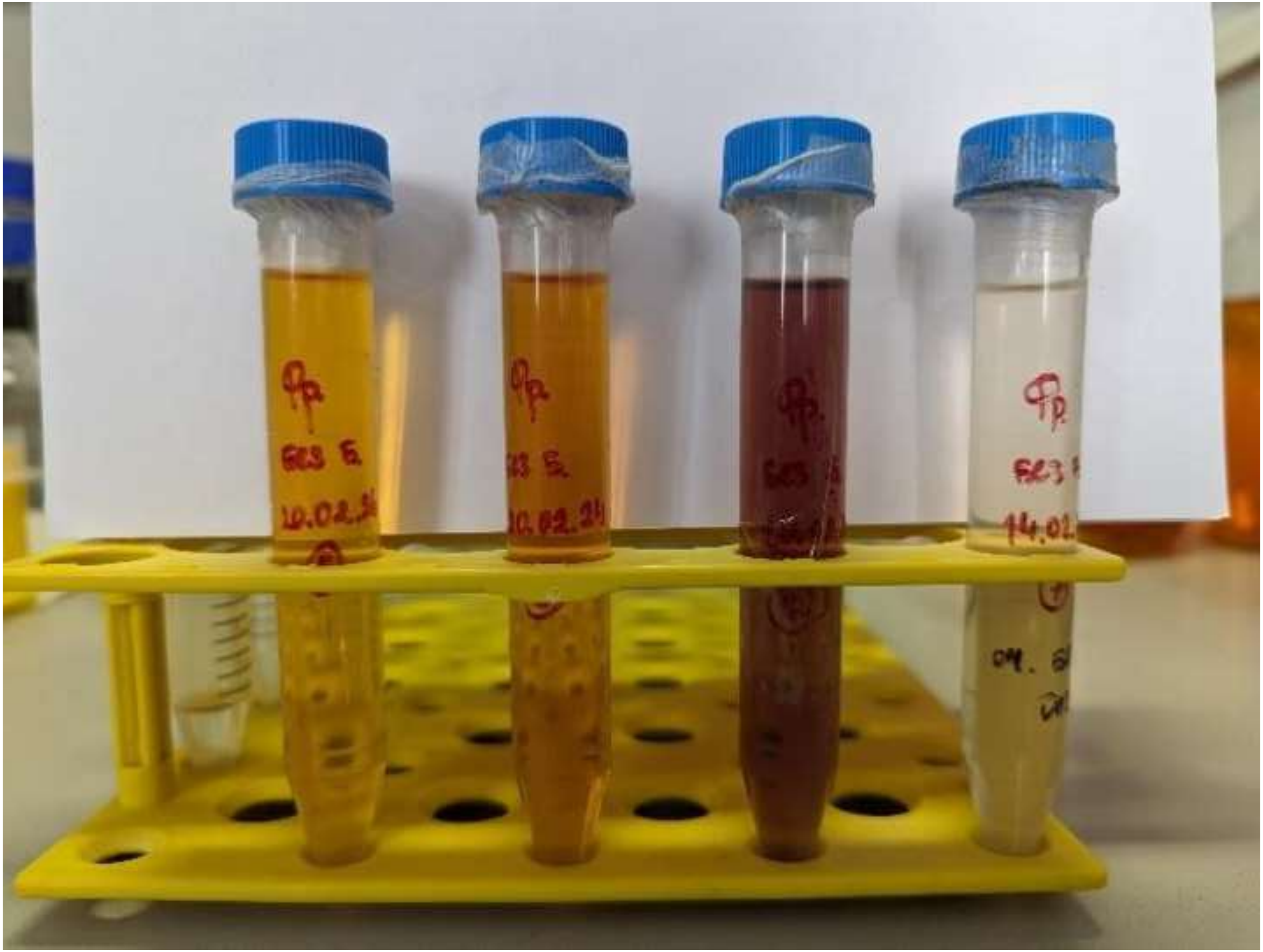

Figure 3

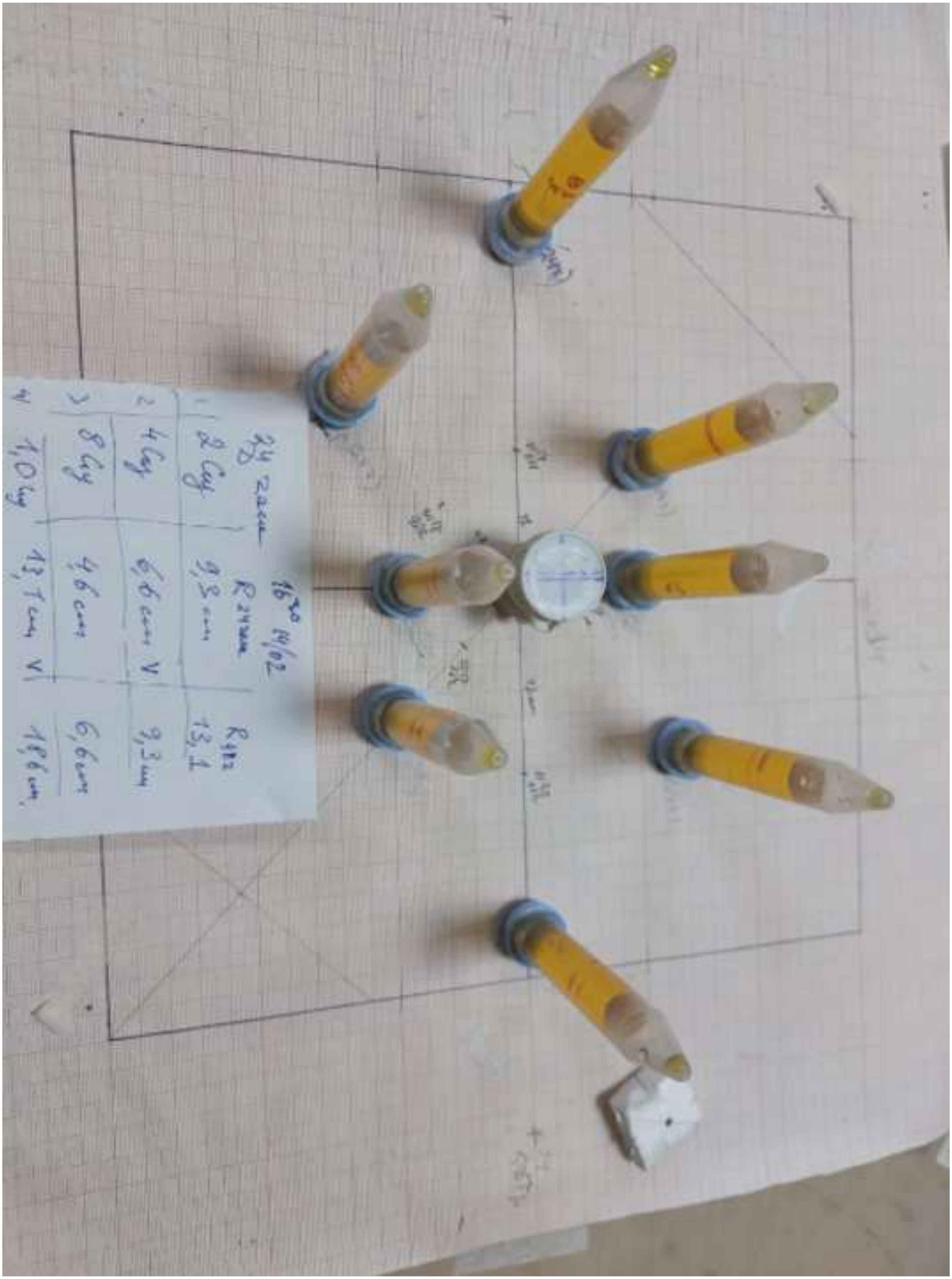

Figure 4

Click here to access/download;Figure;Fig_4.jpg

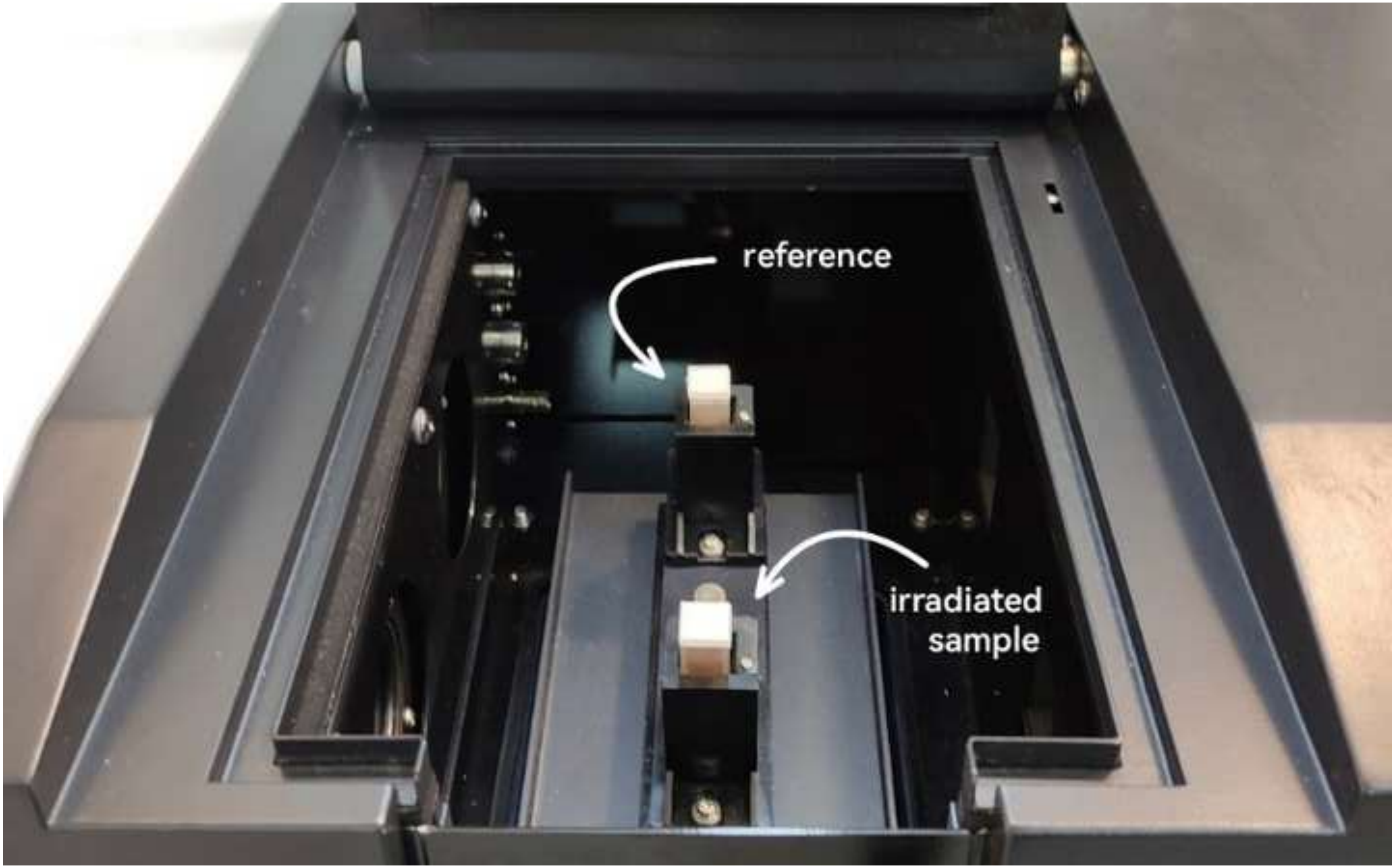

Figure 5

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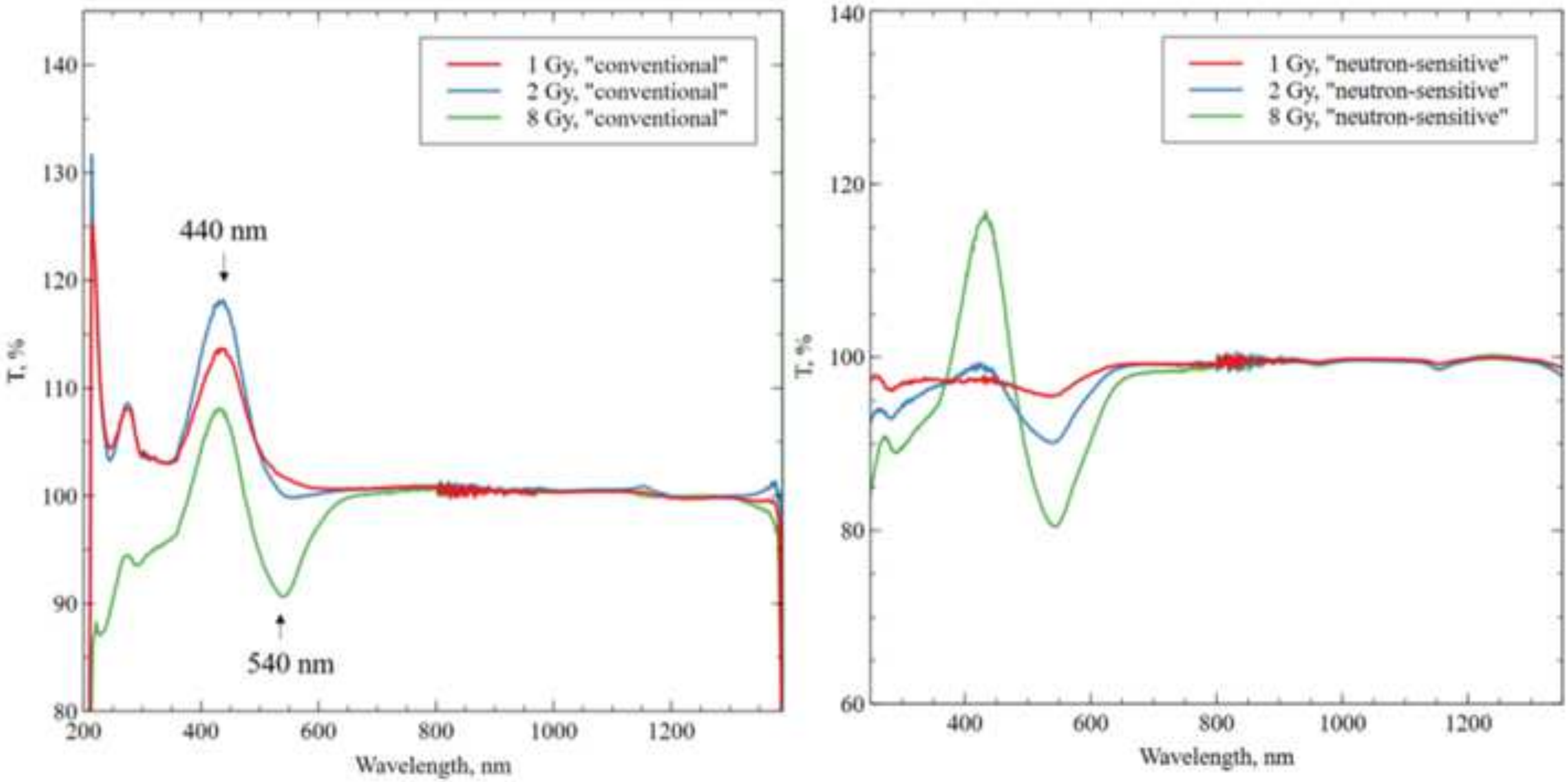

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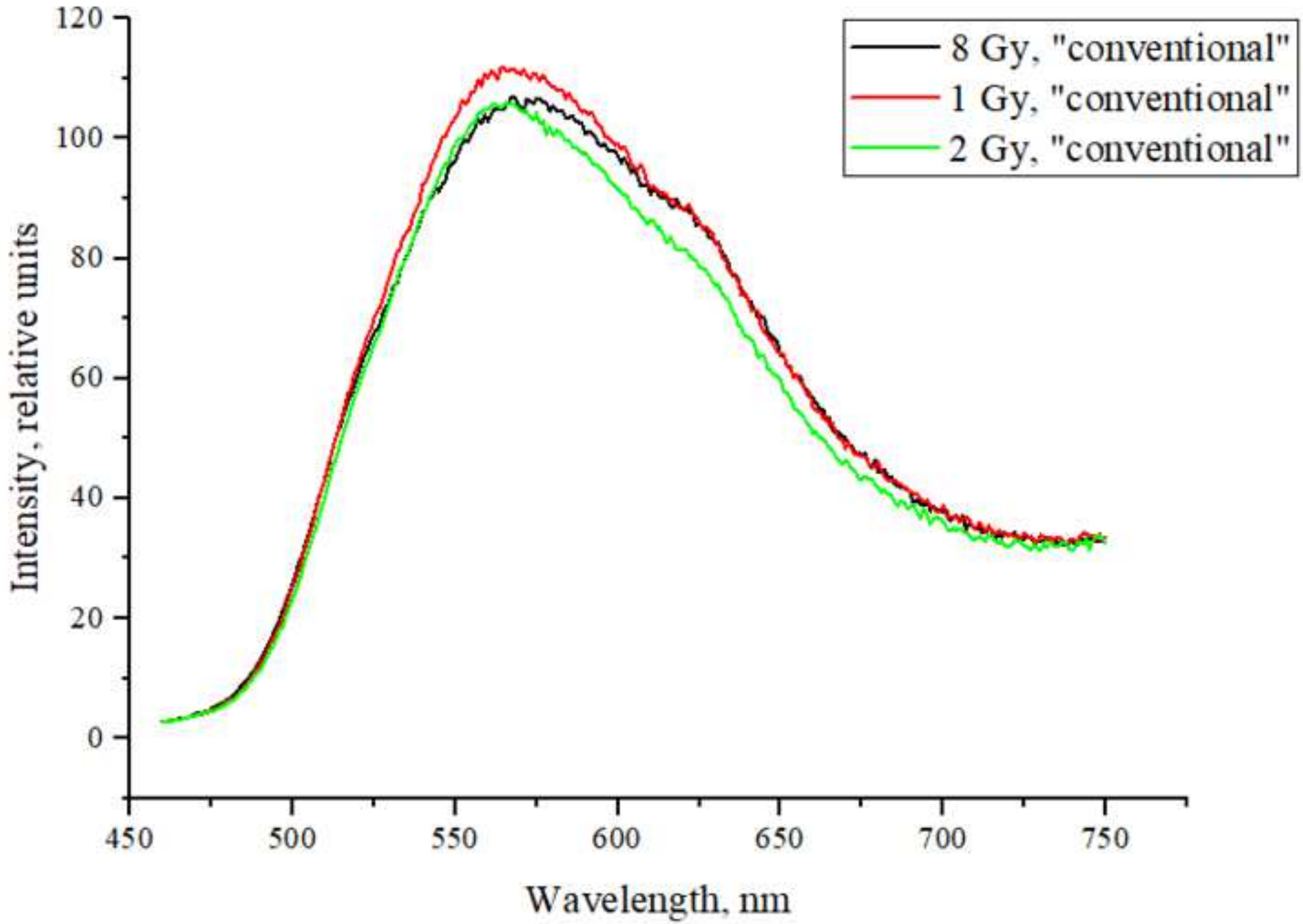

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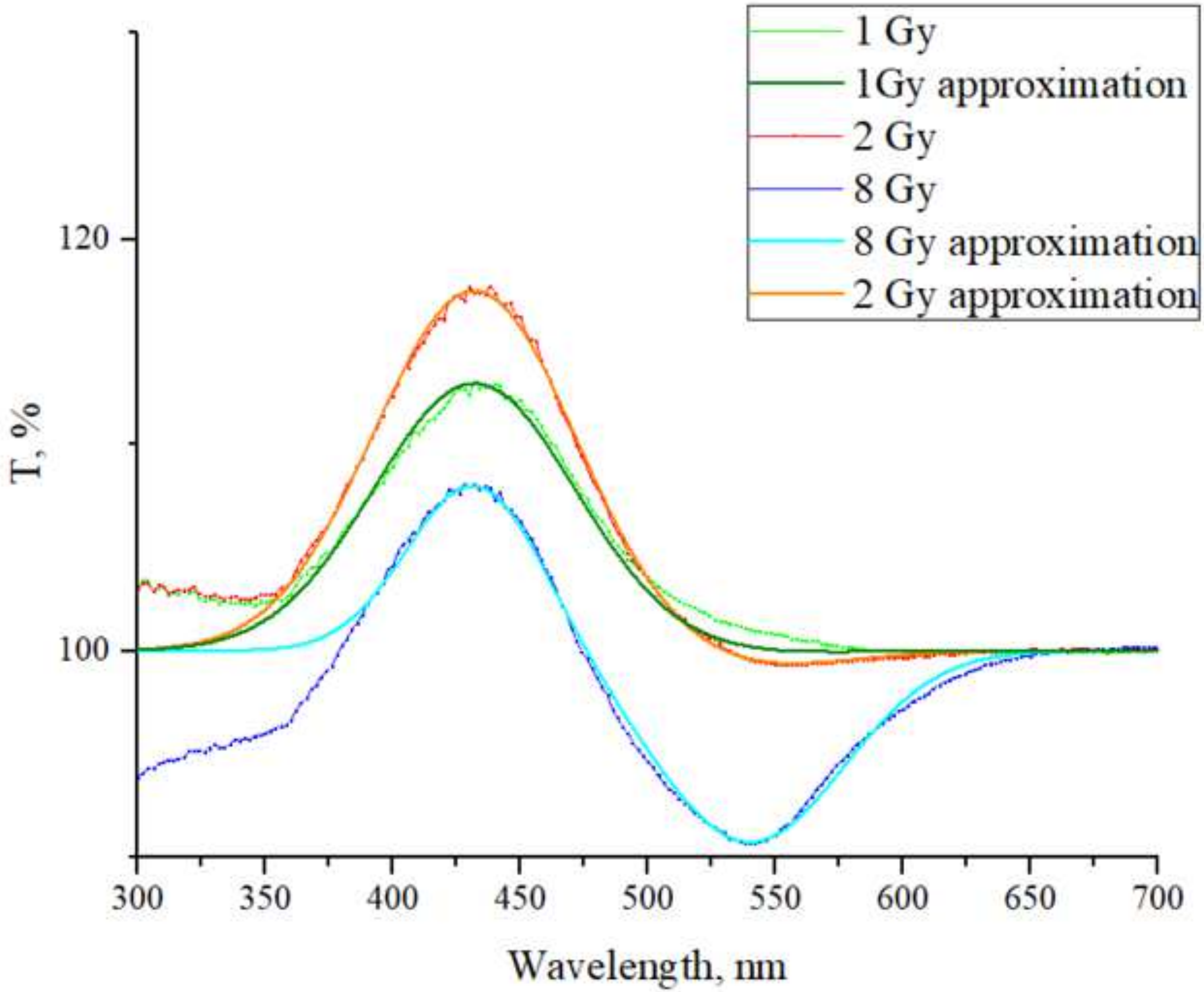
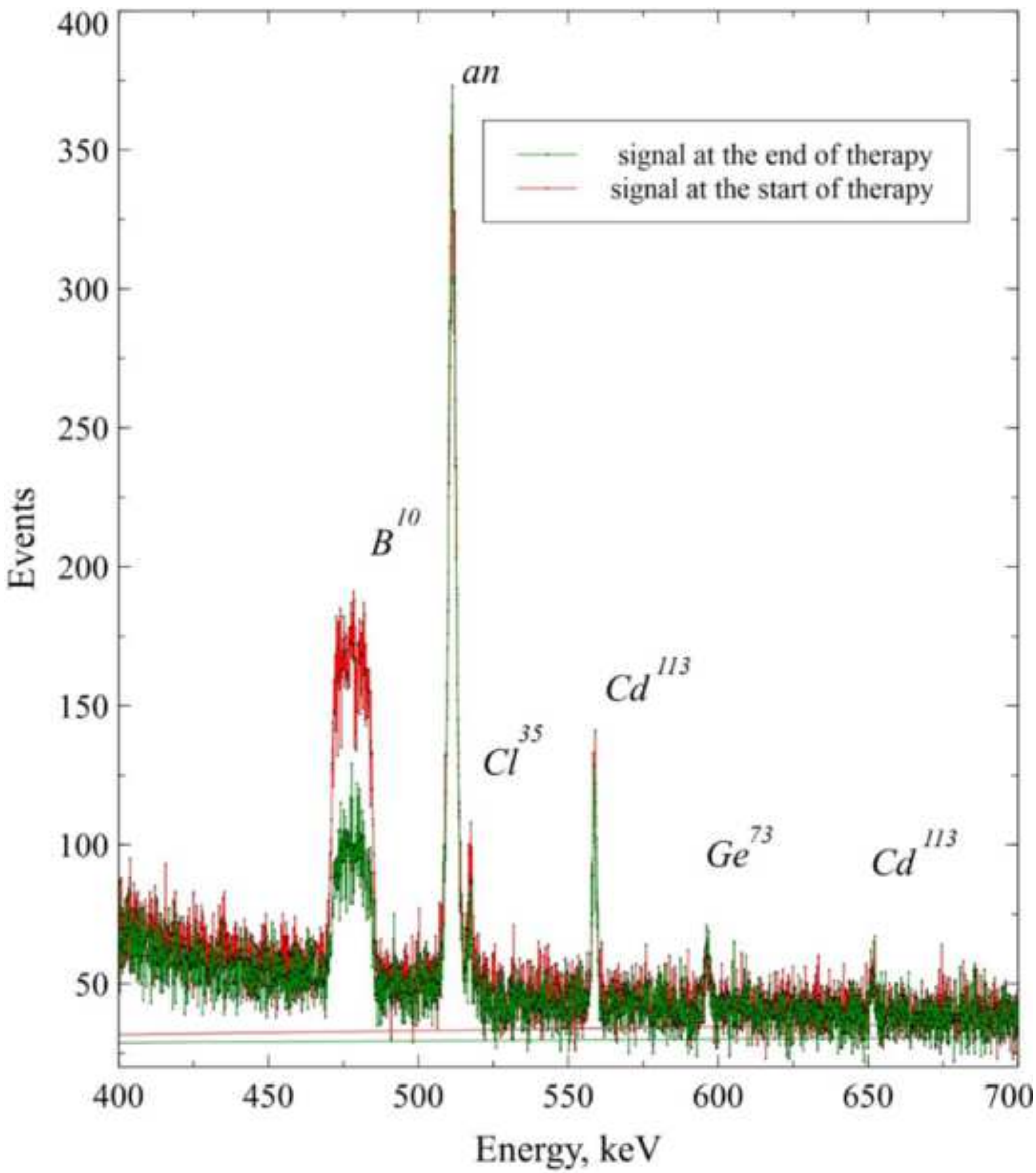

1 Gy
1Gy approximation
2 Gy
8 Gy
8 Gy approximation
2 Gy approximation
120
100
T, %
300
350
400
450
500
550
600
650
700
Wavelength, nm

Figure 11



400
350
300
250
200
150
100
50
Events
400
450
500
550
600
650
700
Energy, keV
an
signal at the end of therapy
signal at the start of therapy
B 10
Cl 35
Cd 113
Ge 73
Cd 113

Figure 9

Click here to access/download;Figure;Fig_9.jpg

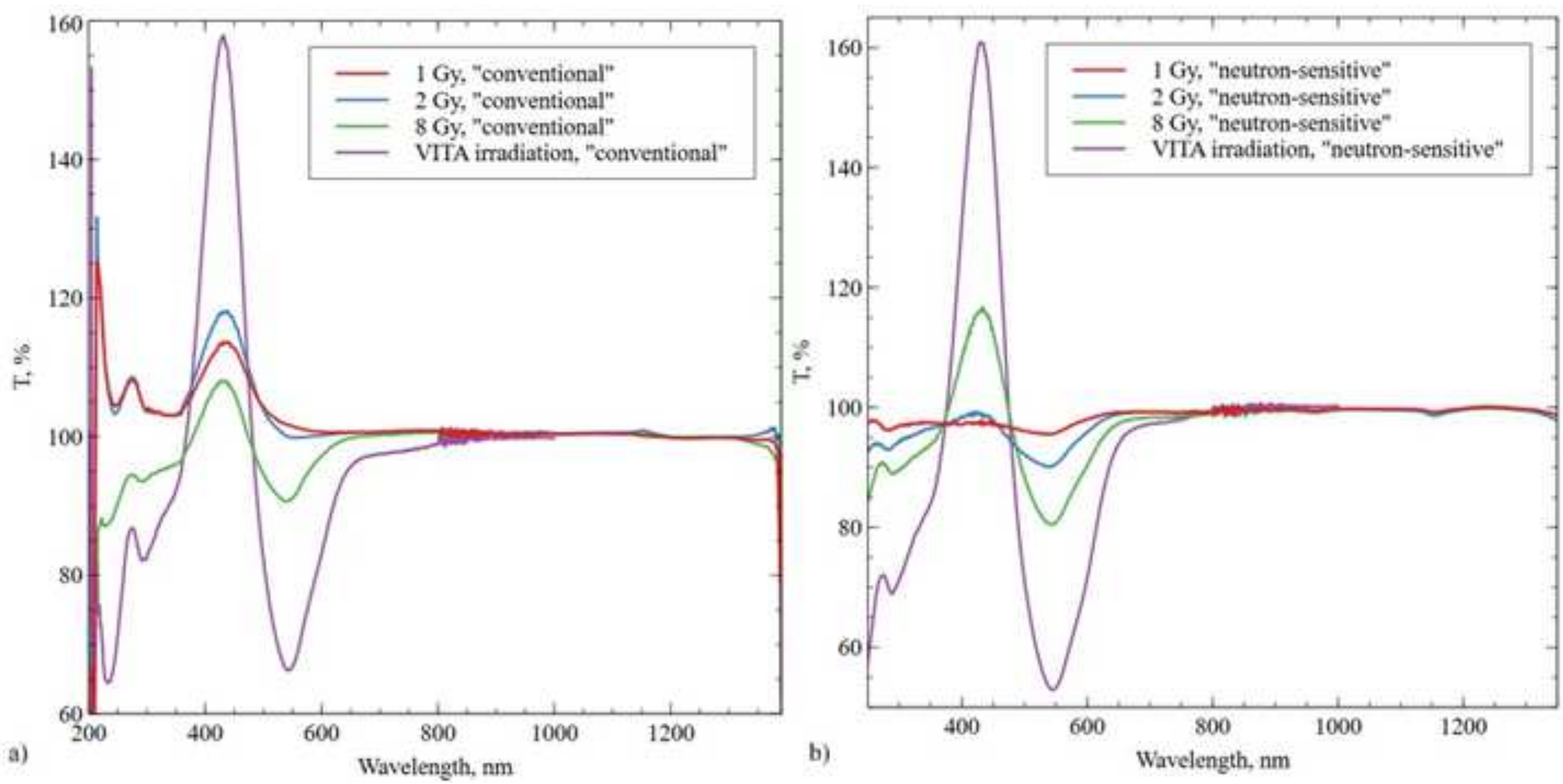


Figure 10

Click here to access/download;Figure;Fig_10.png

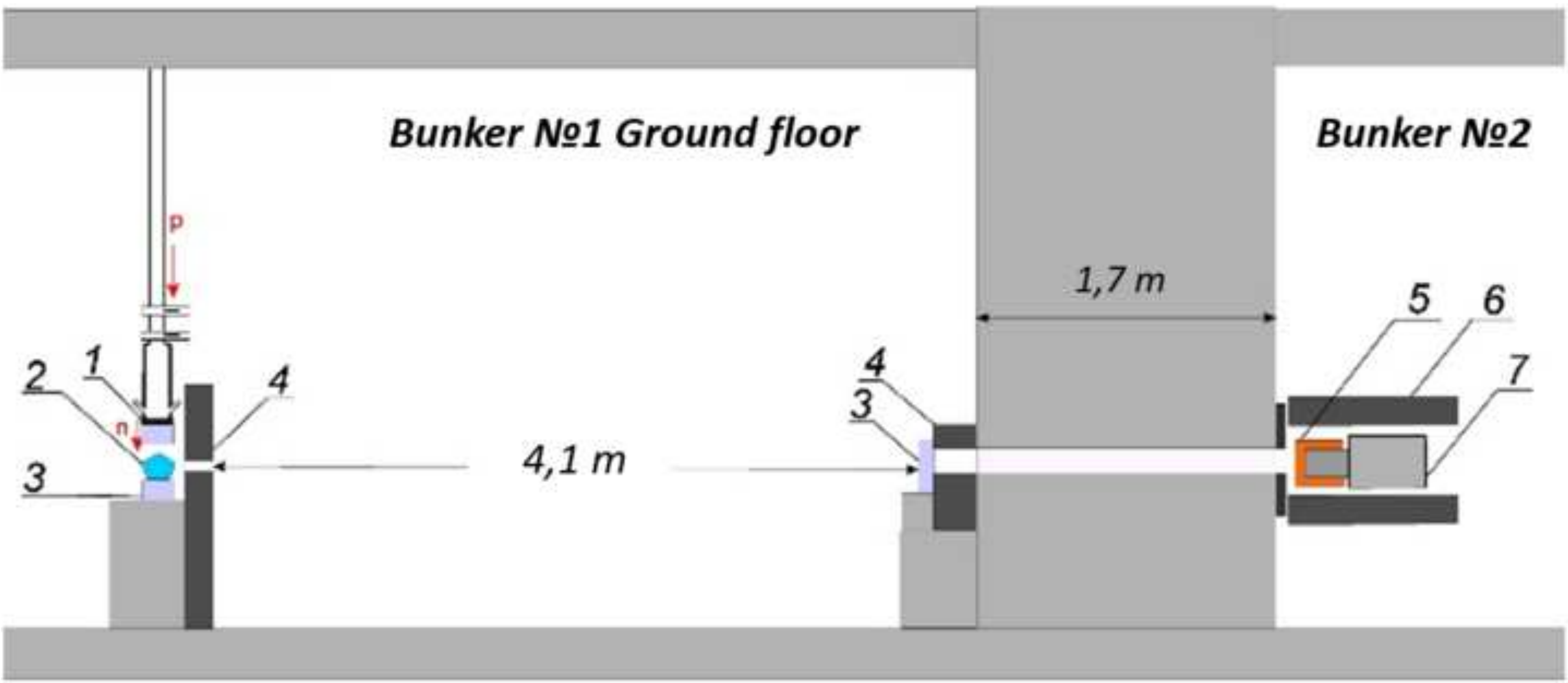


Fig. 1. Absorption spectrum of dosimeters

Fig. 2. Irradiated "conventional" Fricke dosimeters: Dose increases from left to right (far left – unirradiated, far right – 1000 Gy)

Fig. 3. Photo of dosimeter placement for calibration using a ^{137}Cs source

Fig. 4. Arrangement of cuvettes in the Shimadzu UV-3600 Plus spectrophotometer (reference – unirradiated sample)

Fig. 5. Absorption spectra of irradiated "conventional" and "neutron-sensitive" Fricke dosimeters

Fig. 6. Fluorescence spectra of dosimeters excited at 440 nm

Fig. 7. Approximation of the obtained absorption spectra of "conventional" dosimeters

Fig. 8. Calibration of dosimeters using a ^{137}Cs source

Fig 9. Absorption spectra of dosimeters irradiated at the VITA accelerator compared with ^{137}Cs-irradiated samples: a) "conventional" dosimeter, b) "neutron-sensitive" dosimeter

Fig. 10. Experimental setup for boron dose measurement using prompt gamma-ray spectrometry: 1 – lithium target, 2 – animal, 3 – plexiglas, 4 – lead shielding, 5 – cadmium layer, 6 – lead collimator, 7 – gamma-ray spectrometer

Fig 11. Gamma-ray spectrum obtained during BNCT of a laboratory animal

Declaration of interests

☒The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: