

STATEMENT

on a dissertation work for obtaining the educational and scientific degree PhD in professional field 4.1 Physical Sciences (Doctoral Programme Nuclear Physics), in the defense procedure at the Faculty of Physics at Sofia University "St. Kliment Ohridski"

The statement is prepared by: **Assoc. Prof. Dr. Borislav Atanasov Pavlov (Faculty of Physics, Sofia University "St. Kliment Ohridski")**, in his capacity as a member of the scientific jury according to Order No. **RD-38-53/26.01.2024** of the Rector of Sofia University.

Topic of the dissertation work: **"Methods for dosimetric assessment, optimization, and control of radiotherapeutic plans"**

Author of the dissertation work: **Dimitar Rosenov Penev**

1. Description of the presented documents

Dimitar Rosenov Penev has submitted all necessary documents and materials in accordance with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (LDASRB), its Implementing Regulations (IRDASRB), the Regulations on the Conditions and Procedure for Obtaining Scientific Degrees and Taking Academic Positions at Sofia University "St. Kliment Ohridski" (RCPSDA-SU), and the Additional Requirements for Candidates for Obtaining Scientific Degrees at the Faculty of Physics, Sofia University "St. Kliment Ohridski" (ARFP-SU). The documents and materials submitted by the candidate include:

- Dissertation
- Abstracts (one in Bulgarian and one in English)
- Diploma of Higher Education (Master's degree)
- Declaration of authorship
- Comparative table with recommended requirements of the Faculty of Physics, Sofia University "St. Kliment Ohridski"
- Scientific publications (3 papers)
- Curriculum vitae

The documents presented by the candidate for defense comply with the requirements of LDASRB, IRDASRB, RCPSDA-SU, and ARFP-SU.

2. Data on the candidate

From the CV, it is evident that Dimitar Rosenov Penev has been interested in natural sciences since his school years - he graduated from the Natural Sciences and Mathematics High School "Acad. Nikola Obreshkov," (Razgradin) in 2011. He pursued higher education at the Faculty of Physics, Sofia University, completing the Bachelor's program in "Medical Physics" successfully in 2016 and the Master's program again in "Medical Physics" in 2018. Dimitar Penev's professional career is

closely related to the topic of his dissertation. From 2017 to 2018, he worked as a physicist at the Laboratory for Radiation Protection in Medical Radiation at the National Center of Radiobiology and Radiation Protection, and from 2018 to the present, he has been a Medical Physicist at the Laboratory for Clinical Dosimetry and Radiation Protection at the Clinic of Radiotherapy at the University Specialized Hospital for Active Treatment in Oncology (Sofia).

In 2019, he continued his education by starting a doctoral program at the Department of Atomic Physics, Faculty of Physics, Sofia University "St. Kliment Ohridski," in the professional field of Physical Sciences, doctoral program "Nuclear Physics," under the supervision of Prof. DSc. Dobromir Presianov and scientific consultant Dr. Pavel Stavrev.

Dimitar Penev has also undergone additional qualification courses and specializations:

- Course "Interaction of Ionizing Radiations with Matter. Computer Simulations and Models," April 10-13, 2018
- Course "Treatment Planning Systems," EFOMP School for Medical Physics Experts, October 10-12, 2019 (Warsaw, Poland)
- Course "Virtual Regional Training Course on Advanced Treatment Planning Workflow: from Contouring to Plan Evaluation - Prostate and Lymph Nodes," February 6-24, 2023 (Vienna, Austria)

3. The Scientific Achievements of the Doctoral Candidate

The dissertation presented by the doctoral candidate consists of ten chapters. In the first chapter, after a brief introduction, the objectives of the dissertation are formulated. The second chapter presents dosimetry basics and outlines briefly the methodology and regulatory framework necessary for the work of medical physicists in specialized radiotherapy clinics. The third chapter discusses the processes occurring in tumors during irradiation and presents various radiobiological models for assessing the outcome of radiotherapy.

Chapters 4, 5, 6, and 7 present the work and data analysis conducted by the doctoral candidate. The fourth chapter describes the analysis of data from in-vivo experiments with mice (Fisher & Moulder) and in-vitro cell cultures (Tamawski et al.). The study was conducted with statistical data analysis methods and application of various radiobiological models. The fifth chapter also briefly examines the cellular radiosensitivity of heterogeneous tumors. In the sixth chapter, the influence of the fractionation scheme on the probability of tumor control is investigated and discussed. The seventh chapter is dedicated to the influence of dose uncertainty in radiotherapy on the probability of tumor control, and conclusions are drawn that dose uncertainty plays a significant role in the outcome of radiotherapy.

The eighth chapter presents the scientific contributions of the doctoral candidate, along with a list of publications related to the dissertation. In the ninth chapter, some of the computer codes used for the research are provided (as appendices). The dissertation concludes with a bibliography (tenth chapter).

The scientific and scientific-applied results obtained by Dimitar Penev are:

- Verification of the ZMS model using data from in vivo experiments with animals

- Obtaining an assessment of the influence of hypoxia on TCP
- Confirmation by means of TCP models, that tumor control primarily depends on the killing of the most radioresistant tumor cells in the cell conglomerate
- An assessment of the influence of dose uncertainty on the probability of tumor control has been obtained

The dissertation text is structured over 102 pages. The literature used comprises 130 titles, cited in the text. The predominant part of the literature consists of scientific articles, but there are also textbooks and regulatory acts. The volume and nature of the cited literature demonstrate that the doctoral candidate has conducted a detailed study and extensive literary review on the dissertation topic, including the most current literature (the newest article in the bibliography is from 2023). The dissertation includes 27 figures, most of them represent the results obtained by the doctoral candidate. Additionally, the dissertation contains 3 tables and 56 mathematical formulas.

The abstract is presented in 2 languages – Bulgarian (52 pages) and English (49 pages). Both versions are clearly structured and adequately represent the dissertation.

Regarding the dissertation, the doctoral candidate has presented 3 scientific publications (two - Q1 and one - Q2). Dimitar Penev is the first author in one of the scientific publications, which is an indisputable testament to his leading contribution. The scientific publications included in the dissertation work meet the minimum national requirements (according to Art. 2b, para. 2 and 3 of LDASRB) and the additional requirements of SU and the Faculty of Physics for obtaining the educational and scientific degree PhD in professional field 4.1 Physical Sciences. Four reports from international conferences, published as extended abstracts in journals with impact factor, are also presented. From the information in the dissertation and the abstract, it is not clear whether Dimitar Penev personally presented any of these reports.

4. Critical Notes and Recommendations

Overall, the dissertation is well-written and structured, but some minor inaccuracies are encountered. For example, on page 4, " ^{60}Co " is written instead of " ^{60}Co ." Not all quantities used in formula 3 are defined in the text. There is an inaccuracy in formula 4, and a bracket is missing in formula 19. The curves in Figure 5 are referred to in the text as " $(3/5)$ " and " $(5/10)$," while on the graph itself, they are labeled as " $(3/4)$ " and " $(5/9)$," etc. Figures from 8 to 15 would have been better if the data were presented not only with different graphical symbols but also with different colours. In some places in the text, the error is presented with several digits after the decimal point - for example, on page 82, it says: $60.47 \pm 21.57\%$. From the text, it is not clear why such precision is chosen and whether all digits are significant. Overall, the noticed inaccuracies are purely technical in nature and do not diminish the value of the dissertation.

I would recommend Dimitar Penev to continue his scientific research on the same or similar topic.

5. Conclusion

In conclusion, I believe that the volume and quality of the scientific research, the obtained results, and the scientometric indicators meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the regulation for the application of this law, the Regulation on the Conditions and Procedure for Obtaining Scientific Degrees and Taking Academic Positions at SU, as well as the recommended requirements for candidates for obtaining scientific degrees and taking academic positions at the Faculty of Physics, SU "St. Kliment Ohridski".

Dimitar Penev possesses in-depth knowledge and practical skills for conducting independent scientific research. Based on everything written so far, I confidently and without reservations recommend to the esteemed scientific jury to award Dimitar Rosenov Penev the educational and scientific degree PhD in the professional field 4.1 Physical Sciences.

April 21, 2024

Prepared the statement:

/ Assoc. Prof. Dr. Borislav Atanasov Pavlov /