OPINION

on dissertation

for acquiring the educational and science degree of "Ph.D."

in the professional field 4.1. Physical science, Nuclear Physics

the procedure is hold in the Faculty of Physics

of Sofia University "St. Kliment Ohridski" (SU)

by **assoc. prof. Strahil Boychev Georgiev, PhD**

Faculty of Physics, SU

Topic: " Methods for dosimetric assessment, optimization and control of radiotherapy plans"
By Dimitar Rosenov Penev

Dimitar Penev has presented a dissertation in Bulgarian consisting of 102 pages, as well as a Bulgarian (52 pages) and English (49 pages) abstract, which accurately summarizes the content of the dissertation. Mandatory tables for the Faculty of Physics are also included, as per the Rules on the Conditions and Procedure for Acquiring Academic Degrees and Holding Academic Positions in Sofia University "St. Kliment Ohridski". Other documents supporting the candidate's achievements have been submitted in accordance with the requirements.

The documents presented by the candidate meet the legal requirements and the rules of SU.

Dimitar Rosenov Penev graduated from High school "Acad. Nikola Obreshkov", Razgrad in 2011. In 2016, he obtained a bachelor's degree, and in 2018, a master's degree in Medical Physics from the Faculty of Physics at Sofia University. In 2019, he was enrolled as a regular doctoral student in the Department of Atomic Physics at the Faculty of Physics at Sofia University in professional field 4.1. Physical Sciences, in the doctoral program "Nuclear Physics" under the supervision of Professor DSc. Dobromir Presiyanov and with Dr. Pavel Stavrev as his scientific consultant.

During his master's studies, the doctoral student started working in his field as a physicist at the Laboratory of Radiation Protection in Medical Radiation at the National Center of Radiobiology and Radiation Protection from 2017 to 2018. From 2018 until now, he has held the position of Medical Physicist in the Laboratory of Clinical Dosimetry and Radiation Protection at the

Radiotherapy Clinic of the University Specialized Hospital for Active Treatment of Cancer (USBALO) in Sofia.

The primary scientific work of Dimitar Penev is related to the development and study of radiobiological models for the assessment and optimization of tumor irradiation, which is accurately reflected in the dissertation. The dissertation is based on 3 scientific publications in peer-reviewed journals (Q1 and Q2), with the doctoral student being the first and corresponding author in one of the Q1 articles. This fully meets the minimum national requirements and the additional requirements of SU for obtaining the educational and scientific degree of "doctor". Additionally, the candidate is a co-author in 2 other scientific publications (not incl. in the dissertation) visible in the SCOPUS database.

There is no evidence that the material presented in the dissertation has been used in previous procedures for obtaining scientific degrees and academic positions. There is no evidence of plagiarism in the submitted dissertation and abstract according to the legal requirements.

Although the candidate is not required to engage in teaching activities, he actively participates in conducting practical exercises as well as some lectures in the course on "Clinical Dosimetry." The course is mandatory in the curriculum of the Master's program in Medical Physics at the Faculty of Physics.

The main achievements of the candidate are related to the development, application, and analysis of radiobiological models for assessing the probability of tumor control (TCP). His contributions include the development of existing models by incorporating additional parameters that account for previously unaccounted biological effects; application of TCP models to experimental data from other authors for analysis and evaluation of the models; assessment of the influence of various biological and physical parameters on TCP.

The first of the three publications (see Chapter 8 of the dissertation) upon which the dissertation is based, is dedicated to the influence of the uncertainty of the dose on the TCP under various irradiation regimes. Significant influence of this uncertainty has been observed, especially in regimes with TCP in the range of 20-80%. Upper limits of the dose uncertainty have been set, as dose uncertainty greater than 2% leads to unacceptable uncertainties of the TCP estimation for some regimes.

In the second publication (see Chapter 8 of the dissertation), the existing TCP model by Zaider-Minerbo-Stavreva (ZMS) is improved by considering the effect of resensitization on both parameters that account for cell radiosensitivity. The model is validated using experimental data from other authors. A model comparison is made between the conventional irradiation regimen (5 fractions,

5 days, daily) and two extended regimens (again 5 fractions, but with breaks between irradiation days). It is shown that in most cases, extended regimens lead to better results, with improved TCP sometimes exceeding 50% improvement. However, it is found that in some cases conventional irradiation is superior. This underlines the necessity of such models, allowing careful planning of the irradiation regimen for each specific case.

Within the third publication, a Monte Carlo code for assessing the effects of repopulation (parameter λ) and cell death (parameter μ) in TCP modeling is developed and validated. A strong correlation between the parameters describing the two effects is found. However, a thorough analysis shows that the two parameters should be considered separately, rather than as a cumulative parameter (λ-μ), as this can lead to a 10% error in TCP estimation for longer irradiations. It is shown that natural cell death has a non-negligible, positive effect on the outcome of radiotherapy.

I have some minor critical remarks and recommendations for the dissertation. Given the specialized matter and the abundance of abbreviations and parameters in the models, it would have been helpful to compile and present separate lists of abbreviations and parameters for easier reference. There are many long sentences in some places (e.g., page 17 lines 6-10; page 43 lines 1-5), which make them hard to understand. On page 12, the cell survival curve is described in considerable detail, which is undoubtedly important, but adding a figure with an exemplary curve would have been beneficial. In several instances, used quantities are omitted from being defined (e.g., formula 3: Δd_M and ΔD_M; page 48 table). These remarks do not diminish the merits of the dissertation but rather aim to improve it.

My impressions of the candidate during his studies in the bachelor's and master's programs in Medical Physics at the Faculty of Physics are positive – he was a good student: knowledgeable, understanding, and diligent. As a doctoral student and researcher, my impressions are more indirect: precise and consistent in his work as a researcher; and I am receiving good feedback from students as a teacher.

After reviewing the submitted dissertation, abstract, and other materials, and based on the analysis of their significance and the scientific and applied contributions contained therein, **I confirm** that the scientific achievements meet the legal requirements and the Rules of SU **for obtaining the educational and scientific degree of "doctor"**. In particular, the candidate meets the minimum national requirements in the professional field, and no plagiarism has been detected in the submitted dissertation, abstract, and scientific papers.

I give my **positive** evaluation of the dissertation.

Based on the above, I **recommend** to the academic jury to confer **the educational and scientific degree of "doctor"** in the professional field 4.1. Physical Sciences upon **Dimitar Rosenov Penev.**

22.04.2024 г. Opinion by: Strahil Georgiev Digitally signed by Strahil Georgiev Date: 2024.04.22 09:27:34 +03'00' .....

(assoc. prof. Strahil Georgiev, PhD)