STATEMENT

by Prof. Dr. Aneliya Klisarova, MD, PhD, DSc
Head of Department of Nuclear medicine, methabolic therapy and Radiotherapy
Faculty of Medicine
Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

for dissertation thesis for the acquisition of the educational and scientific degree "PhD"
in the area of higher education 7. Healthcare and sports,
professional direction 7.1.
Medicine, scientific specialty "Medical radiology and Roentgenology speciality
(including use of radioactive isotopes)"

Teodora Stoyanova Gugleva, MD,
Department of "Nuclear Medicine, Metabolic Therapy and Radiotherapy"
Faculty of Medicine
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"Investigating the role of deep inspiration breath-hold technique (DIBH) with automatic active breathing device in radiotherapy of left breast to reduce cardiac and pulmonary toxicity"

Dear members of the Scientific Jury,

By order No. R- 109-466 от 06.12.24 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" — Varna and as a chairman of the Scientific Jury, by Decision of the Scientific Jury in accordance with Protocol No. 1/18.12.2024 I was selected to participate with a statement regarding the PhD defense of Teodora Gugleva, MD.

1. **Significance of the scientific subject and formulation of the aim and tasks:**

Adjuvant radiotherapy has a crucial role in the treatment of breast cancer as it reduces the incidence of local recurrences and improves overall survival. However, the proximity of the planning target volume in left-sided breast cancer leads to increased cardiac and pulmonary toxicity. The improved survival rates of breast cancer patients highlight the challenges associated with late toxicity and the necessity of applying treatment techniques that protect organs at risk as much as possible without compromising the delivered dose. One of the techniques used in these cases is irradiation wih Deep Inspiration Breath Hold (DIBH).

The aim of the dissertation is clearly formulated and concerns determining the role and demonstrating the advantages of treatment with DIBH with automatic active breathing device combined with intensity-modulated radiotherapy, compared to free-breathing irradiation with IMRT in patients with left breast cancer. This technique aims to limit doses to the heart and lungs and reduce cardiac and pulmonary toxicity. The tasks, 13 in total, are formulated correctly and align with the stated aim.

2. **Dissertation structure:**

The dissertation thesis follows a classical structure. It is written on 132 pages and includes the following chapters: Introduction, Literature Review, Aim and Tasks, Materials and Methods, Results, Discussion, Conclusions, and Contributions. The thesis contains 16 tables and is illustrated with 44 figures.

The structures of dissertation are well-balanced and the proportions of the individual chapters are balanced. Notably, each part of the dissertation logically follows the stated aim and tasks, and the conclusions naturally arise from the results, statistical data analysis and discussions.

3. **The Ph.D. Candidate's Literature Knowledge:**

The literature review covers 36 pages, where the author provides an in-depth analysis of cardiac and pulmonary toxicity associated with left-sided breast cancer radiotherapy and the current methods for its prevention. The review includes 178 references (3 in Bulgarian), proving the existence of a research gap regarding the

application of DIBH with automatic active breathing device and VMAT to reduce cardiac and pulmonary toxicity in left-sided breast cancer cases.

Given the capabilities of modern equipment and the absence of randomized studies in this area, the methodological level is adequate.

4. Methodological Level and Research Design

The scientific study includes a total of 100 participants, divided into two groups: a control group and a target group.

- The control group includes 30 patients with left-sided breast cancer who had indications for adjuvant radiotherapy. In these group are compared individual dosimetric plans between free-breathing treatment and DIBH with automatic active breathing device using the same irradiation techniques IMRT/ VMAT
- The target group consists of 100 participants (30 patients from the control group and an additional 70 patients) in which evaluated cardiac and pulmonary toxicity during follow-up.

The results were analyzed using appropriately selected statistical methods. The methods and clinical material allowed the author to achieve the research aim, and the tasks were adequately addressed.

5. Correspondence between the aim, results and conclusions:

There is a logical correspondence between the defined aim, the obtained results, the discussion, and the conclusions. The candidate's own results and discussions are presented on 40 pages and are illustrated with tables, figures and statistical analysis. These align closely with the outlined tasks and are comprehensively detailed. The dissertation highlights the significance, advantages, and limitations of using DIBH with automatic active breathing device. The presented data demonstrate the in-depth and detailed analysis conducted by the candidate, particularly in comparing the two dosimetric plans: breath-hold and free-breathing, for the 30 participants in the control group.

6. **Analysis of Conclusions and Contributions:**

The dissertation concludes with 19 conclusions and 11 contributions. The contributions, as per the author's self-assessment, are accepted, highlighting that this is the first study in Bulgarian radiotherapy practice to investigate, report, and prove the benefits of DIBH with automatic active breathing device compared to free-breathing in left-sided breast cancer radiotherapy. For the first time in Bulgaria, a protocol for adjuvant radiotherapy using DIBH for left-sided breast cancer is reported.

7. **Nature of Critical Remarks and Recommendations:**

I have no critical remarks that would cast doubt on the methods, evidence, discussion, or conclusions.

8. **Publications and Scientific Activity**

The research findings have been published in 3 full-text articles and presented in 1 national scientific forum.

Personal Impressions from the Candidate:

Teodora Stoyanova Gugleva, MD is a recognized specialist in radiotherapy. She is among the young professionals who continuously develop and demonstrate interest not only in daily practice but also in innovations in the area. She is professional, collegial, and responsible toward her team at the Clinic of Radiotherapy and the Department of Nuclear Medicine, Metabolic Therapy, and Radiotherapy at the Medical University of Varna, as well as toward colleagues from other clinical specialties.

9. **Conclusion:**

Considering the scientific merits of the dissertation thesis, namely the relevance of the problem, the obtained results, significant conclusions, and contributions, I confidently recommend that the esteemed scientific jury award the educational and scientific degree " PhD " to Teodora Stoyanova Gugleva, MD for her dissertation: "Investigating the role of deep inspiration breath-hold technique

(DIBH) with automatic active breathing device in radiotherapy of left breast to reduce cardiac and pulmonary toxicity".

27.01.2025 Prof. Aneliya Klisarova, MD, PhD, Dsc