To the Chairman of the Scientific Jury, appointed by
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Review

By Prof. Dr. Sonia Borisova Sergieva, Ph.D

Head of the Nuclear Medicine Clinic, Acibadem City Clinic, Tokuda University Hospital

Subject: Dissertation on the topic "The role of positron emission computed tomography (18F-FDG PET/CT) in patients with colorectal carcinoma" in the field of higher education 7.Health and Sports, professional field 7.1.Medicine, scientific specialty "Nuclear Medicine", for the acquisition of the educational and scientific degree " Doctor" to Dr. Gabriela Hristova Mateva, Clinic of Nuclear Medicine, Acibadem City Clinic, University Hospital "Mladost".

Brief biographical data:

Dr. Mateva graduated from the Faculty of Medicine of Sofia University "St. Kliment Ohridski" in 2016. In the same year, she started working at the Nuclear Medicine Clinic of Acibadem City Clinic Mladost, where she was enrolled as a resident in 2018 and obtained a specialty in Nuclear Medicine in 2022. Dr. Mateva has many active participations in scientific forums in the country and abroad, as well as specializations in the Netherlands, Austria, Greece, Romania, Italy and Spain. Her scientific interests are in the field of nuclear oncology, with a focus on solid tumors - mainly colorectal carcinoma and theranostics, as well as in the field of nuclear cardiology.

The topic of the dissertation is very relevant. Colorectal carcinoma is among the leading malignant diseases in terms of incidence and mortality worldwide, but despite the improvement of screening and therapeutic approaches, survival remains unsatisfactory, especially in patients with advanced disease. This necessitates the need to search for new therapeutic options and improve diagnostic methods. The application of 18F-FDG PET/CT in patients with colorectal carcinoma has not yet been fully studied. The only established indication in the ESMO and NCCN recommendations is to clarify the cause of an increase in the level of carcinoembryonic antigen (CEA) with negative results from other imaging studies. The dissertation work is aimed at investigating the applicability of the method in real clinical practice, but also at less well-studied specific indications for PET/CT in patients with colorectal carcinoma, e.g. application in local therapeutic techniques, such as radiosurgery and radiofrequency ablation of liver lesions and search for relationships between metabolic parameters and serum tumor markers.

The dissertation is structured in accordance with standard requirements, is written in 142 pages and contains the following main parts:

- Title page – 1 page
- Table of contents – 1 page
- List of abbreviations used – 1 page
- Literature review – 35 pages
- Goal and objectives – 1 page
- Materials and Methods – 8 pages
- Results and discussion – 77 pages
- Conclusions – 2 pages
- Contributions – 2 pages
- Publications related to scientific work – 1 page
- Bibliography – 14 pages

The dissertation is well illustrated with 65 figures and 9 tables, presenting the obtained results in a very informative manner.

The bibliography includes 145 literature sources, most published in the last 10 years, with 15 of the sources being by Bulgarian authors. The literature review is developed in-

depth and comprehensively. The epidemiology, anatomical and pathophysiological foundations of the disease, screening and diagnostic methods, histological and immunohistochemical diagnosis, prognostic and predictive biomarkers, serum tumor markers, principles and recommendations for the application of imaging diagnostics, therapeutic approaches and strategies, as well as the currently available literature data on the application of PET/CT in patients with colorectal carcinoma are examined in detail.

Based on the conclusions from the literature data, Dr. Mateva has formulated the goal of her work precisely and clearly and has set 4 tasks for its implementation in order to determine the application of 18 F-FDG PET/CT in patients with colorectal carcinoma. The clinical material includes 110 patients with colorectal carcinoma, divided into 4 groups according to the tasks set:

- First group – 50 patients with colorectal carcinoma, in whom the application of 18F-FDG PET/CT in determining the stage and restaging of the disease, place in the diagnostic algorithm, role in choosing a therapeutic approach was studied
- Second group – 26 patients with metastatic liver lesions from colorectal carcinoma, in whom the use of 18F-FDG PET/CT for planning and evaluating the effectiveness of radiosurgery was investigated
- Third group - 23 patients, of whom 16 had a primary focus other than the colon, to study the application of 18F-FDG PET/CT to assess the effectiveness of radiofrequency ablation of metastatic liver lesions
- Fourth group – 18 patients in whom the relationship between metabolic parameters measured by 18F-FDG PET/CT and serum levels of tumor markers (CEA and CA 19-9) in patients with metastatic colorectal carcinoma was studied.

The results are presented in detail, analyzed in relation to each specific task set in the dissertation work, the advantages and disadvantages of the imaging method in each specific situation are shown. Where possible, the corresponding sensitivity, specificity and diagnostic accuracy were calculated and compared with the reference imaging method CT and CEUS. The role of various metabolic parameters as predictive markers for the success of various therapeutic approaches is discussed.

The results are discussed in a comparative aspect in the context of published data and analyses of other authors who have worked on the relevant topics. The main contributions of the dissertation are the following:

- For the first time in Bulgaria, an in-depth study of the application of 18F-FDG PET/CT in patients with colorectal cancer has been carried out - clinical indications, its place in the diagnostic algorithm and the ways in which it is combined in practice with other imaging methods.
- The role of PET/CT in the use of local therapeutic techniques to assess their effectiveness is analyzed in detail. Recommendations are presented with a contribution to global practice, emphasizing the importance of an individualized approach and the integration of data from clinical status, laboratory parameters, and imaging studies.
- For the first time in Bulgaria, the role of 18F-FDG PET/CT in planning and monitoring the effectiveness of radiosurgery (SBRT) in patients with metastatic liver lesions from colorectal carcinoma has been studied. A number of metabolic parameters measured with PET/CT have been analyzed in order to establish dependencies and determine threshold values with predictive value for the final therapeutic outcome.
- For the first time in the country, the application of 18F-FDG PET/CT to assess the effectiveness of radiofrequency ablation of liver metastases has been studied and its diagnostic accuracy has been compared with that of contrast-enhanced ultrasound (CEUS).
- A strong correlation between metabolic tumor volume and CEA levels has been established for the first time, as a direct individual function of this volume for each patient. This finding provides a basis for using CEA as a reliable laboratory marker for monitoring therapeutic response.

In relation to the topic of the dissertation, a total of 2 real publications and 5 participations in prestigious European congresses have been presented, with abstracts published in journals with an impact factor.

Conclusion:

Dr. Mateva's dissertation on the topic "The role of positron emission computed tomography (18F-FDG PET/CT) in patients with colorectal carcinoma" possesses all the necessary qualities and meets the legal requirements for acquiring scientific degrees and titles.

The topicality of the topic of the presented dissertation, the way in which the dissertation candidate approached it, as well as the original contributions of the work, are reasons for me to confidently give my *positive assessment and a recommendation to the other esteemed members of the Scientific Jury to award* the educational and scientific degree "Doctor" to Dr. Gabriela Hristova Mateva.

Prepared by: Prof. Sonia Borisova Sergieva, Ph.D.

1.10.2025