# STATEMENT

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According to order № P-109-473 / 05.11 2021 of the Rector of the Medical University - Varna, I have been selected to prepare a Statement on the dissertation of Dr. Tsvetelina Yordanova Petrova-Georgieva.

Regarding a dissertation on a topic:

ROLE OF 18F-FDG PET / CT IN THE DIAGNOSTIC ALGORITHM IN MALIGNANT EPITHELIAL TUMORS OF THE HEAD AND NECK
for awarding the educational and scientific degree "Doctor" in the scientific specialty Medical Radiology and Radiology (including the use of radioactive isotopes) in the field of higher education "Health and Sports", professional field 7.1. "Medicine".

Author: DR. TSVETELINA YORDANOVA PETROVA-GEORGIEVA

1. Significance of the problem and formulation of the goal and tasks:
Malignant epithelial tumors of the head and neck is a heterogeneous disease characterized by complex clinical and pathological manifestations. It accounts for approximately 90% of all head and neck cancers. Over the last decade, significant progress has been made in understanding the epidemiology, pathogenesis and treatment of this type of cancer.
In our country, the kead nd neck tumors are most common in people of active age, 45-55 years, which makes early diagnosis, prevention, treatment, follow-up and recovery after treatment an extremely serious challenge. The selection of a treatment strategy depends directly on the correct and timely diagnosis, staging, monitoring and evaluation of the effect of treatment with imaging methods.
For these reasons, the dissertation of Dr. Tsvetelina Georgieva is of current importance, both from a theoretical and practical point of view and has a contribution to the strategy in the diagnosis and therapy of these tumors.

2. Structure of the dissertation:

The dissertation is presented on 121 pages and contains 12 figures, 28 tables, 21 graphs and 8 diagrams. The structure of the dissertation is well balanced, the proportions between the individual sections are observed. I want to pay attention to the chapters own results, where the author very clearly and in detail proves the implementation of the tasks. Each results section is followed by a discussion and recommendations for practice.

3. Literary awareness of the dissertation:
The literature reference includes titles, of which 2 in Cyrillic and 124 in Latin. The literature review is written with skill. The scientific publications on the topic are critical and the advantages of 18F-FDG PET / CT and the main problems in the diagnosis of Head and neck tumors are presented.

The wide information with which the author works, the correct use of the scientific terminology and the full and correct citation of the authors of the scientific publications in the field are impressive. It is worth noting the strict focus of the review on the goal and objectives of the dissertation, which presents Dr. Georgieva as a multifaceted excellently trained researcher.

It should be noted that 53% of these publications are from the last 10 years.

The aim of the dissertation is a logical continuation of the literature review, namely: to determine the role of 18F-FDG PET / CT in the diagnostic algorithm in malignant epithelial tumors of the head and neck.

There are six main tasks, which are formulated clearly and precisely. The tasks are specific, well planned and correspond to the set goal, which shows the good theoretical preparation and mastery of the problem by the dissertation.

1. To investigate the role of 18F-FDG PET / CT in detecting an unclear primary focus in patients with proven metastatic cervical lymph nodes from squamous cell carcinoma.

2. To study the role of 18F-FDG PET / CT in the staging of malignant epithelial tumors of the head and neck.

3. To evaluate the use of 18F-FDG PET / CT to detect local recurrence in malignant epithelial tumors of the head and neck.

4. To investigate the use of 18F-FDG PET / CT to assess treatment response in malignant epithelial tumors of the head and neck.

5. To investigate the role of 18F-FDG PET / CT in the follow-up of malignant epithelial tumors of the head and neck.

6. To evaluate the role of 18F-FDG PET / CT as a method for detection of second primary tumor and distant metastases in patients with malignant epithelial tumors of the head and neck.

## 4. Methodical level and design of the dissertation:

The Material and Methods section presents the patients included in the scientific work with correctly defined inclusion criteria and description of 18FDG-PET and the used methods for comparison and verification of the results. The dissertation is based on a retrospective analysis of 205 patients who underwent 308 18F-FDG PET / CT tests at the Clinic of Nuclear Medicine at the University Hospital "St. Marina" Varna in the period from January 2015 to December 2017. Patient follow-up was performed and additional verification of surgical interventions and imaging studies for a minimum of 12 months was included.

The methodology of performing the set tasks is described in detail, accurately and skillfully. The criteria for visual and semi-quantitative assessment in the evaluation of therapy and follow-up of the studied patients with malignant epithelial tumors of the head and neck are defined in detail and precisely.

The statistical analysis of the obtained results was performed using modern appropriate methods. Sensitivity, specificity, accuracy, positive and negative predictive value in different groups of studied patients were calculated.

## 5. Correspondence between the goal, the results and the conclusions

There is a logical correspondence between the set goal, the obtained results, the discussion and the conclusions made.

The results of the dissertation work are described exhaustively in 6 sections, which purposefully and correctly prove the set tasks. The results are presented in detail, after each section there is a discussion of the obtained results, their comparison with those of other imaging methods, with the data from the scientific literature and histological verification.

6. Analysis of the conclusions and contributions:

Based on the obtained results, the dissertation synthesizes 11 conclusions, which are written specifically and clearly and are related to the set goal and the developed tasks. They define the main benefits of 18F-FDG PET / CT in patients with tumors with unnoun origine, staging of patients with head and neck tumors, detection of recurrence, evaluation of therapeutic response, follow-up and detection of a second occult primary tumor. Sensitivity, specificity and accuracy in different groups of patients are determined, visual and semi-quantitative evaluation criteria are defined.

I accept the presented contributions of the dissertation, which can be defined as theoretical and scientific-applied.

1. For the first time in Bulgaria the role of 18F-FDG PET / CT for localization of primary tumor focus in patients with tumors with unnoun origine and histologically proven metastatic cervical lymph nodes from squamous cell carcinoma was studied.

2. For the first time, quantitative and qualitative assessment of the metabolic response locoregionally is applied in patients with HNT after the end of RT (with or without systemic therapy) using the following three methods: 5-point visual (Deauville) scale, 3-point visual scale and the semi-quantitative method with measurement of SUVmax value. Thresholds were established for each of the three methods for reliable categorization of patients into two groups: complete and incomplete metabolic response in the head and neck.

2A. 18F-FDG PET / CT should be used to assess the metabolic response locoregionally in HNT after RT (with or without ChT / targeted therapy), to select patients in two groups: complete and incomplete metabolic response.

2B. For the first time, the locoregional metabolic response from HNT treatment was assessed using a 5-point visual (Deauville) scale, with a cut off value for a complete metabolic response below grade 3 and for an incomplete metabolic response grade 3 and higher. Introduction of a 5-point visual (Deauville) scale for reliable and objective assessment of the metabolic response after treatment of HNT and referral to a further therapeutic approach.

2B. For the first time, the metabolic response from head and neck treatment in HNT was assessed by a second visual scale - in 3 grades: reporting a complete metabolic response from treatment below grade 2 and an incomplete metabolic response at grade 2 and above. The introduction of a 3-point visual scale to assess the metabolic response from head and neck treatment, which is easily applicable and highly reliable, can rule out persistence of a vital tumor, according to the degree of 18F-FDG accumulation locoregionally.

2D. A cut off value of SUVmax-2.45 was found, at which patients with HNT can be divided into two groups according to the locoregional response after treatment: with complete and incomplete metabolic response.

3. Survival was determined until the onset of the first local recurrence in patients with HNT followed by Control 18F-FDG PET / CT- from 21.8 months.

4. Mean survival to first control 18F-FDG PET / CT was calculated in follow-up of patients with complete and incomplete metabolic response to primary HNT after treatment. Patients

with a complete metabolic response to the primary tumor should later undergo a first follow-up PET / CT scan after an average of 22 months, and patients with an incomplete metabolic response to the primary HNT after an average of 16 months.

5. Survival of patients with HNT up to first control 18F-FDG PET / CT with remission data (DFS) and survival without locoregional recurrence (LRFS) was calculated, respectively, 25.8 months and 23 months.

Based on the obtained results and the conclusions from them, valuable recommendations for clinical practice have been made.

In connection with the dissertation Dr. Georgieva has 3 real publications in which she is the first author and 4 reports at scientific forums, all related to the topic of the dissertation.

The dissertation is written clearly and concisely, in good literary Bulgarian.

The abstract is written concisely and adequately reflects the content of the dissertation.

The author has complied with all the recommendations I made in advance when discussing the dissertation.

Conclusion:

The dissertation of Dr. Tsvetelina Georgieva is an in-depth and precisely conducted scientific development.

The dissertation is a topical work with scientific and applied value. The goal and tasks are precisely set, the results obtained are convincing, the conclusions are clearly formulated and comprehensive. The contributions have theoretical and practical value. The dissertation covers the quantitative indicators for acquiring the educational and scientific degree "Doctor" and fully meets the requirements of the Law for Developement of the Academic Staff in the Republic of Bulgaria and the Regulations for its implementation and the rules for the development of the academic stuff at the Medical University-Varna for acquiring the degree "Doctor".

Having in mind the above, I give a positive assessment of the dissertation of Dr. Tsvetelina Yordanova Petrova-Georgieva and recommend to the esteemed Scientific Jury to award her the scientific and educational degree "DOCTOR".

02.12.2021