

**To the Chairman of the Scientific Jury,**

**determined by Order No. P-109-258/06.06.2025**

**To the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov"- Varna**

**Prof. Dr. Dimitar Raykov, MD**

**MU-Varna**

**I hereby submit: STATEMENT**

**On the competition for the academic position of "Associate Professor" in the field of higher education 7 "Health and Sports", professional field 7.1 "Medicine", scientific specialty "Nuclear Medicine", announced in the State Gazette, issue No. 30 of 08.04.2025**

**for the needs of the Department of "Nuclear Medicine, Metabolic Therapy and Radiotherapy", Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" Varna**

**By order No. R-109-258 of 06.06.2025 of the Rector of MU-Varna and by decision of the first meeting of the Scientific Jury, I have been appointed to participate with an statement in this competition.**

## STATEMENT

by Prof. Dr. Antonia Dencheva Tsonevska, MD

Scientific specialties – Medical radiology (radiotherapy and nuclear medicine), Oncology

The statement has been drawn up in accordance with the requirements of ZRASRB and PPZRASRB - Section III - Conditions and procedure for occupying the academic position of "docent"

In the aforementioned competition, announced in the State Newspaper No. 30 dated 08.04.2025, the only candidate participating was Senior Assistant Dr. Marina Dyankova, MD. in the Department of Nuclear Medicine, Metabolic Therapy and Radiotherapy, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov"-Varna".

All submitted documents and materials of the candidate have been prepared in accordance with the requirements of the PPZRASRB of MU-Varna

### 1. Professional and academic development

Dr. Marina Dyankova has been working as a doctor in the Clinic of Nuclear Medicine and Metabolic Therapy, University Hospital "St. Marina" - EAD, Varna since 2015. Since 2018, she has been a part-time assistant at MU-Varna. In 2019, she acquired a specialty in Nuclear Medicine. In 01.2020, she held the position of assistant at the Department of Imaging Diagnostics, Interventional Radiology and Radiotherapy at the Medical University-Varna. In 06.2022. acquired educational and scientific degree "Doctor", scientific specialty "Medical Radiology and Radiology (incl. use of radioactive isotopes)" after successful defense of a dissertation "<sup>68</sup>Ga-PSMA PET/CT in prostate carcinoma. Advantages and possible diagnostic errors." In 06.2023 she holds the position of Chief Assistant Professor at the Department of Imaging, Interventional Radiology and Radiotherapy at the Medical University - Varna.

She actively participates in scientific forums in Bulgaria and abroad, continuing education courses conducted by IAEA and EANM in Latvia and Bulgaria, annual European congresses EANM, ESOR, ESHI, BAR, as well as the international symposium WARMTH in Finland. She actively participates in seminars of the European School of Nuclear Medicine, organized by EANM, ESMIT, as well as in annual online courses for continuing education of medical specialists organized by SNMMI, EFRS, CHILI. She is an active participant in scientific forums: national and international conferences and congresses. She is a member of WiN Bulgaria - Association "Women in the Nuclear Industry - Bulgaria", European Society for Hybrid, Molecular and Translational Imaging (ESHI), European School of Radiology (ESOR), as well as EANM. Dr. M. Dyankova participates in various international trainings and shares her experience with medical students and X-ray laboratory technicians. Her professional interests are in the field of prostate carcinoma, Langerhans' histiocytosis,

multiple myeloma, ovarian carcinoma, hyperparathyroidism and malignant melanoma. She is fluent in Russian, Ukrainian and English.

During her work in the field of nuclear medicine, Dr. Dyankova has established herself as a respected colleague, with high professionalism, with a desire for innovation, initiative, efficiency, a sense of responsibility, communication and efficiency.

## 2. Evaluation of scientific and research activities:

In the current competition for the academic position of "associate professor", senior assistant Dr. M. Dyankova participated with 37 scientific works (full-text articles and reports), most of which were published after the successful defense of the dissertation on the topic "68Ga-PSMA PET/CT IN PROSTATE CARCINOMA. ADVANTAGES AND POSSIBLE DIAGNOSTIC ERRORS" and acquisition of the educational scientific degree "doctor".

The total publication activity for participation in the competition for the academic position of "associate professor" is high and includes:

Full-text articles - 15, of which 11 are published in refereed publications, which are also indexed in world-renowned databases of scientific information;

Published summaries of reports from scientific forums in our country and abroad - 25;

Participation in scientific forums in our country and abroad, with a program - 25.

In the presented materials, senior assistant professor Dr. M. Dyankova is the first author of 12, second author of 5 and third and subsequent author of 20 scientific papers. 33 titles are published in publications, refereed and indexed in world-renowned databases of scientific information.

The presented list of citations covers the requirements for holding the academic position of "associate professor". The citations are in our and foreign journals, which proves a significant contribution and relevance of the scientific interests against the background of the high publication activity.

The academic reference for fulfilling the minimum national requirements and the requirements of the Regulations for holding academic positions at MU-Varna, shows 230 points - results, covering the scientometric requirements.

The total impact factor / IF is 369.979, which proves the significance of the scientific publications.

### Assessment of contributions

In the presented scientific production of Senior Assistant Dr. Marina Dyankova, MD, she reaches a number of conclusions that contribute to nuclear medicine science and practice.

The contributions of Dr. Dyankova's scientific production are in the following scientific areas: nuclear medicine and Oncology

1. studies and scientific papers related to prostate cancer

2. studies and scientific papers related to other oncological diseases .

Other areas of nuclear medicine

## 1. studies and scientific papers related to prostate cancer

Scientific and applied contributions derived from the conducted studies:

1. For the first time in nuclear medicine practice in Bulgaria, the application of the newly introduced hybrid imaging method  $^{68}\text{Ga}$ -PSMA PET/CT in a large cohort of patients with biochemical recurrence of PC after radical therapy has been studied. The prognostic factors for positivity of PSMA-PET results, the factors related to the frequency of detection, as well as the advantages of the method compared to CT have been determined. The application of PSMA PET/CT in patients with biochemical progression after radical prostatectomy in the wide range of tumor marker values (with an emphasis on low PSA levels) has been studied. The influence of PSA values on the sensitivity and frequency of PSMA-PET detection was analyzed, the relationship between PSA levels and the frequency of detection of recurrent PC at different locations was determined, as well as the relationship between Gleason score and the frequency of detection, the respective locations of recurrent PC, ADT/hormonal therapy performed and PSA values.
2. The application of PSMA-PET in the initial regional nodal (N) and distant metastatic (M) staging of patients with primary PC at moderate and high risk before radical therapy was studied. The advantages of PSMA-PET over conventional CT were determined.
3. An in-depth study of the application of the method in patients with ISUP grade 5 was performed for the first time in nuclear medicine practice in the country, the characteristics of nodal and bone metastasis, the relationship between the frequency of detection for different locations of malignant involvement by PC and PSA values, as well as the clinical T stage were analyzed.
4. The role of  $^{68}\text{Ga}$ -PSMA PET/CT in the study of patients with primary PC at moderate and high risk before radical therapy is emphasized in comparison with conventional imaging methods (CT, MRI and CS) for the assessment of regional nodal (N) and distant metastasis (M status), the factors associated with the frequency of detection of regional LV and distant metastatic lesions are determined. For the first time in nuclear medicine practice in Bulgaria, the influence of  $^{68}\text{Ga}$ -PSMA PET/CT on (N, M) staging has been analyzed. An in-depth study of the different anatomical patterns of metastatic involvement of the primary, as well as recurrent PC in  $^{68}\text{Ga}$ -PSMA PET/CT scanning has been performed (in a total of 386 patients).
5. The parameters of  $^{68}\text{Ga}$ -PSMA PET/CT were analyzed: detection rate, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy, including the risk of false-positive and false-negative results in the different diagnostic groups of patients.
6. A thorough study of the relationship between positive/pathological PSMA PET/CT results and PSA values, Gleason score/ISUP grade, clinical T stage and other factors was performed in patients with BHR after radical therapy (n=133), with biochemical progression after RP (n=144), as well as with primary PC (n=109) in a total of 386 patients.
7. In order to optimize the interpretation of PSMA-PET results, a thorough analysis of possible diagnostic errors was performed, including different variations of physiological PSMA-activity, pathological expression of the PSMA-antigen not associated with PC, as well as false-negative findings.

To the applied clinical-diagnostic contributions, I include the proposed recommendations for clinical practice based on the conducted studies:

1. Following the principles of the individual approach, the implementation of 68Ga-PSMA PET/CT is justified in patients with biochemical progression after RP at low values of the tumor marker - PSA.
2. The obtained results demonstrate the high potential of the hybrid method PSMA PET/CT to replace both conventional imaging modalities (bone scintigraphy and computed tomography/CT) in the initial staging of patients with high-risk PC, which will therefore optimize the diagnostic algorithm of primary PC and reduce the radiation burden in these patients.
3. In order to exclude possible false-negative results, PSMA PET/CT in patients with ISUP grade 5 should be interpreted with caution, especially in patients with neuroendocrine differentiation of PC, as well as in restaging patients with BPH with elevated PSA levels and negative PSMA PET/CT scan. In patients with ISUP grade 5, especially in those with proven absent PSMA expression, following the principles of the individual approach, an alternative imaging study for the evaluation of high-risk PC should be considered: 18F-FDG PET/CT or 68Ga-DOTA-TATE PET/CT.
4. The interpretation of 68Ga-PSMA PET/CT with the presence of 68Ga-PSMA PET/CT-positive findings in patients after radical prostatectomy and undetectable PSA should always include a comprehensive assessment of the clinical case - risk group, PSA values and the degree of PSMA accumulation in the lesions. In these situations, further clarification of positive PSMA findings is necessary before a decision is made to change the therapeutic approach.
5. 68Ga-PSMA-11-PET/CT has a crucial role in determining the therapeutic plan - salvage radiotherapy in men with early biochemical recurrence of prostate carcinoma after radical prostatectomy. It has been proven that PSMA PET/CT can significantly contribute to a personalized approach in radiotherapy planning, which can improve progression-free survival.

## 2. Studies and scientific papers related to other oncological diseases

The most important scientific contributions from these studies are:

- Evaluation of the diagnostic and clinical value of [18F]FDG PET/CT in patients with malignant melanoma in the follow-up after definitive treatment of first local recurrence, as well as for the early detection of operable disease progression.
- The key role of 18F-FDG PET/CT in the diagnosis of POEMS syndrome has been proven by providing an anatomical and metabolic image of the whole body.
- The parameters of the 18F-FDG PET/CT imaging method have been studied in patients with multiple myeloma referred for staging due to clinical/laboratory data of relapse or progression after treatment. The calculated parametric indicators provide evidence in support of the possible successful application of 18F-FDG PET/CT in patients referred for restaging in case of suspected progression or relapse after treatment.
- The effectiveness of physical examination/endoscopy was compared with the effectiveness of FDG-PET/CT for detecting recurrences of head and neck squamous cell carcinoma after treatment, demonstrating high sensitivity and negative prognostic value for detecting local recurrences even in cases of diagnostic doubt after physical examination/endoscopy.
- The effectiveness of 18F-PET/CT for detecting metachronous/synchronous primary tumors in patients with head and neck carcinoma (HNC) was assessed.

- The role of 18F-FDG PET/CT for determining/changing the therapeutic plan in patients with malignant melanoma at different clinical stages was studied, demonstrating high sensitivity for detecting cutaneous melanoma, due to the high glucose metabolism of the lesions, visualization of the whole body, including the extremities, allowing the detection of small subclinical metastases.
- The role of 18F-FDG PET/CT in patients with an unknown primary tumor suspected of multiple myeloma has been investigated as a non-invasive and highly sensitive whole-body examination that allows not only the detection of the primary tumor, but also its simultaneous staging and determination of a site for targeted biopsy.
- The application of 18F-FDG PET/CT to assess the metabolic activity of osteolytic lesions in patients with newly diagnosed multiple myeloma as a predictive factor for overall survival has been investigated.

The scientific, applied and methodological contributions can be attributed to:

- IMPETUs criteria have been proposed for simplification and standardization in the interpretation of 18F-FDG PET/CT scans in multiple myeloma and have been found to provide a significant prognostic index when the utilization of the radiotracer remains high in the bone marrow and/or focal hypermetabolic lesions, especially after therapy. In 18F-FDG PET/CT for the evaluation of multiple myeloma, recommendations have been made for the use of the Total body 18F-FDG PET/CT protocol in the presence of clinical suspicions, patient complaints of pain in the lower extremities or suspicions of diffuse bone involvement, which will allow the timely detection of occult osteolytic lesions in long bones with high fracture risk and, accordingly, the avoidance of possible surgical interventions. The application of 18F-FDG PET/CT for the evaluation of pathological fractures in multiple myeloma has been studied. The application of 18F-FDG PET/CT for the assessment of metabolic activity of osteolytic lesions in patients with multiple myeloma after treatment for the assessment of tumor vitality has been studied. 18F-FDG PET/CT is recommended as a standard technique for the assessment and monitoring of metabolic response to therapy in patients with multiple myeloma.
- The role of 18F-FDG PET/CT for the detection of late complete metabolic response, assessed using two scans with different time intervals in patients with malignant epithelial tumors of the head and neck after radiotherapy with or without systemic chemotherapy.
- The application of 18F-FDG PET/CT in pulmonary Langerhans cell histiocytosis has been studied and the method is recommended as a valuable and promising imaging method for staging/initial assessment of PLHC, as well as for restaging, with a view to monitoring the therapeutic response.
- The irreplaceable role of 18F-FDG PET/CT as a restaging method, taking into account progression in a patient with malignant peripheral nerve sheath tumor (MPNST), developed on the basis of neurofibromatosis, has been assessed, not only due to the possibility of whole-body scanning, but also due to its high sensitivity and specificity for detecting relapse and distant metastases.
- The application of 68GA-DOTATATE PET/CT in monitoring the effect of the treatment of a patient with a neuroendocrine tumor of the pancreas has been studied.
- The role of 18F-FDG PET/CT in the diagnosis and evaluation of an incidentally diagnosed secondary skin lesion in a patient with a tumor of unknown origin (TOU) during the COVID-19 pandemic was investigated. The advantages of 18F-FDG PET/CT in determining an appropriate biopsy site and accurately staging a tumor of unknown origin were reported.
- The application of 99mTc MDP whole-body bone scintigraphy in the rare McCune-Albright syndrome was studied. McCune-Albright syndrome (MAS) is a rare genetic disorder caused by a mutation in the GNAS1 gene, affecting the bones, skin, and endocrine system. The key



role of <sup>99</sup>Tc MDP whole-body bone scintigraphy in the evaluation of patients with MAS syndrome is reflected, which can assess the spread of the disease in a single study, allowing better monitoring and prognostic assessment of the patient, as well as determining the subsequent therapeutic approach.

–The role of <sup>18</sup>F-FDG-PET/CT for guiding biopsy in the diagnosis of primary extranodal diffuse large B-cell lymphoma of the bone was investigated.

–The role of <sup>18</sup>F-FDG PET/CT in the detection of leptomeningeal metastases was investigated as a useful imaging method for detecting leptomeningeal carcinomatosis in a patient with extraosseous plasmacytoma.

–The possible diagnostic errors in the interpretation of <sup>18</sup>F-FDG PET/CT examination of patients with metachronous tumors were investigated.

#### Other

–The role of <sup>18</sup>F-FDG PET/CT for detection of FDG-active lymph nodes in response to SARS-CoV-2 vaccination has been studied” in order to optimize the clinical interpretation of the results of hybrid scans, which determine the subsequent therapeutic approach in patients with diagnosed cancer.

### 3. Assessment of teaching and clinical activities.

#### Teaching activities

A certificate from MU-Varna, issued on 14.04.2025, shows that Dr. Dyankova has teaching experience as an assistant and chief assistant at the university for 5 years.2 months. 10 days. Dr. Dyankova conducts exercises for Bulgarian and foreign students in fourth year medicine, as well as X-ray laboratory assistants (Medical College Varna). Participates in the examination committees of the above-mentioned students.

The academic workload of Dr. M. Dyankova exceeds 100 academic hours per academic year, which meets the requirements for participation in the competition.

She actively participates in the basic course in nuclear medicine with lectures.

Dr. Dyankova actively participates in a number of educational and scientific forums in our country with international participation, as well as events organized by the Clinic of "Nuclear Medicine and Metabolic Therapy" University Hospital "St. Marina" - Varna and Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

She is a member of the Academic Council of the Faculty of Medicine of Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

#### Clinical work

Dr. Dyankova actively participates in the daily work of the Clinic of "Nuclear Medicine and Metabolic Therapy" of the University Hospital "St. Marina" Varna. Since 2015, she has been part of the team of the Nuclear Medicine Clinic, successfully applying the knowledge gained in the specialty. She works diligently in close collaboration with colleagues from all clinics of the University Hospital "St. Marina" Varna, as well as in the country.

4. General assessment of the candidate's compliance with the mandatory conditions and mandatory quantitative criteria and scientometric indicators for holding the academic position, according to the ZRASRB and PPZRASRB.

After detailed familiarization with the scientometric indicators and quantitative criteria in the documents of Dr. Marina Dyankova, I believe that they meet the national requirements for holding the academic position "Associate Professor".

#### CONCLUSION:

Dr. Marina Dyankova possesses the qualities of an excellent professional and a profound and promising scientist, who, along with her practical activities, successfully poses and solves current and important scientific problems.

Considering the criteria of the ZRASRB and PPZRASRB, as well as the documentation presented by Dr. Marina Dyankova, I can state that Dr. Dyankova is a qualified specialist in nuclear medicine and a reliable and proven scientist and researcher.

The analysis of the scientific research and teaching qualities of Dr. Dyankova, as well as her scientific potential, give me reason to propose to the esteemed scientific jury to vote positively for her election to the academic position of "associate professor" for the needs of the Department of "Nuclear Medicine, Metabolic Therapy and Radiotherapy", Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov"-Varna

30.07.2025

Prof. Dr. A. Tsonevska, MD

Заличено на основание чл. 5, §1, б. „В“ от Регламент (ЕС) 2016/679
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