To the Chairperson of the Academic Committee
Faculty of Medicine
Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

Opinion Statement

Regarding the competition for the academic position of "Associate Professor" in the field of higher education area 7 "Healthcare and Sports", professional field 7.1 "Medicine", scientific specialty "Nuclear Medicine", announced in the State Gazette, issue no. 30 of April 8, 2025, for the needs of the Department of Nuclear Medicine, Metabolic Therapy and Radiotherapy, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

Submitted by:

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By Rector's Order No. R-109-258/06.06.2025 of MU–Varna, I have been appointed as a member of the Academic Committee. According to Protocol No. 1 from the first meeting of the Committee, I have been assigned to prepare an opinion statement on the procedure for awarding the academic position of "Associate Professor" in the specialty "Nuclear Medicine".

The only candidate participating in the announced competition is Chief Assistant Dr. Marina Ivanova Dyankova, MD, PhD, from the Department of Nuclear Medicine, Metabolic Therapy and Radiotherapy, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

Brief Biographical Information

Dr. Marina Dyankova was born on February 3, 1985, in Odesa, Ukraine. She graduated in medicine with honors in 2008 and specialized in Family Medicine (2008–2010). Since 2013, she has held a recognized medical qualification in Bulgaria.

She worked at MC "Clinica Nova" – Varna (2014–2015), and since 2015 she has been part of the team at the Nuclear Medicine Clinic of University Hospital "St. Marina" – Varna. In 2018, she became a part-time assistant, and in 2020 a full-time assistant at the Department of Imaging Diagnostics and Radiotherapy at MU–Varna.

In 2019, she obtained her specialty in Nuclear Medicine, and in 2022 defended her doctoral dissertation titled: "Ga-68 PSMA PET/CT in Prostate Carcinoma: Advantages and Possible Diagnostic Pitfalls." Since June 2023, she has been a Chief Assistant in the same department.

She actively participates in scientific forums and trainings organized by EANM, ESOR, SNMMI, IAEA, as well as in international congresses and courses. She is a member of the Bulgarian Society of Nuclear Medicine, WiN Global – Bulgaria, EANM, ESHI, and ESOR. She teaches medical students and radiology technologists.

Her scientific interests include prostate carcinoma, Langerhans cell histiocytosis, multiple myeloma, ovarian carcinoma, hyperparathyroidism, and malignant melanoma. She is fluent in Russian, Ukrainian, and English.

Scientometric Indicators

In the current competition for the academic position of "Associate Professor," Chief Assistant Dr. M. Dyankova participates with 37 scientific works (full-text articles and conference proceedings), demonstrating a deep personal interest in the diagnostics of prostate carcinoma using Ga-68-PSMA PET/CT.

Total publication activity includes:

- 15 full-text articles (11 in peer-reviewed/indexed journals, two of which have an impact factor), and
- 22 abstracts from the annual EANM congress.
  Dr. Dyankova is the first author of 12 papers, second author of 5, and co-author in 20.
- In journals with an impact factor, Dr. Dyankova has 34 publications and abstracts, with a total Impact Factor (IF) of 369.979.

- Citations: 5, of which 4 are in articles published in peer-reviewed journals. The citations appear in both Bulgarian and international journals, meeting and exceeding the requirements for the academic rank of Associate Professor.

I. Scientific Contributions Related to the PhD Dissertation

In her research, Dr. Dyankova presents for the first time in Bulgaria a large-scale clinical experience with Ga-68 PSMA PET/CT in several key areas, both in the diagnostic and therapeutic processes for patients with prostate cancer (PCa).

The study covers a total of 386 patients, stratified into three main subgroups:

- Patients with biochemical recurrence (BCR) after radical prostatectomy (n=133),
- Patients with biochemical progression after radical prostatectomy (n=144), and
- Patients with primary prostate cancer before radical treatment (n=109).

The study focuses on detection rates, prognostic factors, diagnostic limitations, and the potential for optimizing the clinical algorithm for PCa using PSMA PET/CT.

1. **Biochemical Recurrence and Low PSA Levels**
   For the first time in the country, the application of Ga-68 PSMA PET/CT was studied in a large cohort of BCR patients after radical therapy, including those with low PSA levels. Prognostic factors for a positive imaging result were identified—PSA levels, Gleason score, ISUP grade, previous hormonal therapy, and clinical T-stage. A direct correlation was found between PSA levels and detection rate, as well as between recurrence localization and prior treatment. The advantages of PSMA PET/CT over conventional CT were highlighted, particularly in patients with low PSA values where standard methods fail to detect recurrent disease.
2. **Initial Staging of Primary Prostate Cancer**
   PSMA PET/CT demonstrated significant superiority in initial regional (N) and distant metastatic (M) staging in moderate- to high-risk primary PCa patients. Comparison with conventional imaging modalities (CT and bone scintigraphy) showed higher detection rates and accuracy, justifying the potential for PSMA PET/CT to replace both methods

and reduce radiation exposure. The study examined the impact of PSMA PET/CT on staging and its role in individualized treatment planning.

3. **Diagnostics in Patients with ISUP Grade 5**

   An in-depth analysis was conducted on PSMA PET/CT in patients with ISUP grade 5—the most aggressive histological category. This group showed the highest detection rate, particularly for distant metastases. However, the study also identified diagnostic limitations such as false negatives in cases with neuroendocrine differentiation and absent PSMA expression. Based on these findings, specific recommendations were made for alternative imaging, including ^{18}F-FDG PET/CT or ^{68}Ga-DOTA-TATE PET/CT.

4. **Diagnostic Performance and Statistical Indicators**

   The study evaluated and compared key diagnostic parameters of Ga-68 PSMA PET/CT: detection rate, sensitivity, specificity, positive and negative predictive value, and overall accuracy. For the first time in Bulgarian clinical practice, these metrics were compared across different patient subgroups, with the best performance observed in ISUP grade 5 patients.

5. **Limitations and Possible Diagnostic Errors**

   Major factors contributing to false-positive and false-negative results were analyzed, including physiological variations in PSMA expression, non-specific uptake in inflammatory conditions, and heterogeneity in PSMA expression. Guidelines were proposed for result interpretation to minimize diagnostic errors.

6. **Role in Therapy Response Assessment**

   Ga-68 PSMA PET/CT was applied in evaluating response to androgen deprivation therapy in hormone-sensitive PCa. A heterogeneous therapeutic response was confirmed, with the most pronounced effect in lymph node and bone metastases, compared to the primary tumor. Metastatic lesions with persistent PSMA expression post-ADT may aid in selecting patients eligible for localized treatment in oligometastatic disease.

7. **Role in Planning Salvage Radiotherapy**

   The influence of PSMA PET/CT on salvage radiotherapy planning was studied in BCR patients with low PSA ($\leq$ 0.5 ng/ml) after radical prostatectomy. The method

demonstrably supports personalized radiotherapy planning, which can lead to prolonged progression-free survival.

Key Practical Contributions Related to Ga-68 PSMA PET/CT in Clinical Practice:

- PSMA PET/CT is a highly sensitive and specific method, especially in high-risk PCa patients and those with ISUP grade 5.
- The method is recommended for BCR even at low PSA levels, taking into account risk factors and histological features.
- PSMA PET/CT has the potential to replace standard staging methods in primary PCa.
- In cases with negative PET/CT results but high PSA and/or ISUP 5, increased clinical vigilance is necessary due to the risk of false-negative findings.
- The results confirm the significant role of PSMA PET/CT in personalized diagnostics and treatment planning for prostate cancer.

II. Scientific Contributions of the Publications and Conference Presentations Submitted for the Competition

The leading and original scientific contributions, evident from the articles and scientific forum presentations submitted by Dr. Marina Dyankova for the competition, are primarily related to her extensive experience with both ^{18}F-FDG PET/CT and ^{68}Ga-PSMA.

Five of the full-text publications, four abstracts published in peer-reviewed journals, and one article in a non-indexed journal are dedicated to Dr. Dyankova's work on the role of ^{68}Ga-PSMA in prostate cancer.

The studies involving ^{18}F-FDG PET/CT cover several key topics: multiple myeloma, malignant melanoma, POEMS syndrome, head and neck squamous cell carcinoma, neuroendocrine tumors (NETs), and Langerhans cell histiocytosis (LCH). A brief summary of the contributions is as follows:

1. **Cutaneous Melanoma** – Demonstrated the high diagnostic value of ^{18}F-FDG PET/CT in follow-up after initial regional recurrence, with emphasis on early detection of operable progression and superiority over conventional imaging methods.

2. **POEMS Syndrome** – PET/CT plays a key role by providing comprehensive anatomical and metabolic visualization, supporting diagnosis through detection of bone lesions and associated findings.
3. **Multiple Myeloma** – Established as a valuable modality for restaging, enabling detection of extramedullary infiltration and showing high prognostic value. The metabolic activity of lesions, assessed via SUVmax, is confirmed as a predictor of overall survival in newly diagnosed cases.
4. **Head and Neck Squamous Cell Carcinoma** – PET/CT demonstrates higher sensitivity and prognostic value than physical examination and endoscopy for detecting recurrence. The technique has been shown to have extremely high accuracy (99%) for identifying metachronous/synchronous tumors in this patient group.
5. **Importance of Brain Inclusion in PET/CT Protocol** – Emphasized the diagnostic significance of including the brain in PET/CT protocols for oncological patients to enable early diagnosis and improved prognosis.
6. **Occult Tumors in Myeloma Patients** – PET/CT shows high diagnostic value in patients with suspicious osteolytic lesions, assisting in staging and biopsy site selection.

The review of published abstracts includes a series of clinical cases and studies illustrating the diagnostic potential of modern nuclear medicine imaging modalities such as PET/CT and scintigraphic techniques. These clinical cases demonstrate the multifaceted role of nuclear imaging in contemporary oncology and non-oncology diagnostics.

Summary of Key Scientific Contributions:

1. **PSMA PET/CT** demonstrates sensitivity not only for prostate cancer but also for other neoplasms with elevated PSMA expression. A case of incidental synchronous rectal carcinoma emphasizes the need for histological verification of incidental findings and opens discussion on the potential use of PSMA-targeted therapy in colorectal cancer.
2. **FDG PET/CT** is confirmed as an essential tool for staging, monitoring, and restaging rare and diagnostically challenging conditions, such as PLCH, MPNST, primary osseous non-

Hodgkin lymphoma, and leptomeningeal metastases. It has high diagnostic value for biopsy site selection and therapy response assessment.

3. **Ga-68 DOTATATE PET**/CT proves highly effective in diagnosing and monitoring pancreatic neuroendocrine tumors, providing new opportunities for personalized therapy.
4. Bone scintigraphy with 99mTc MDP demonstrates its unique role in the comprehensive assessment of **McCune-Albright syndrome**, enabling evaluation of fibrous dysplasia distribution and supporting therapeutic decision-making.
5. **Rare cases and artifacts** have been reported, including increased radiopharmaceutical uptake in the hemidiaphragm post-pneumonectomy and a complex case of osteomyelitis in a patient with multiple myeloma—situations requiring a high level of expertise in interpretation.
6. **Differential diagnosis in Ga-68 PSMA PET/CT** remains challenging due to non-specific PSMA expression in both benign and malignant lesions. It is noted that the degree of radiopharmaceutical uptake is not always indicative of etiology, requiring an individualized clinical approach.
7. The **diagnostic value of PET/CT in cancers of unknown primary origin** is underscored, especially under resource constraints during the COVID-19 pandemic.

III. Teaching and Clinical Activity

- Dr. Dyankova has been teaching since 2018 as a part-time assistant, and since 2023 she has been a Chief Assistant at the Department of Imaging Diagnostics, Radiotherapy and Interventional Radiology. She conducts practical classes and lectures for medical students and radiology technologists (over 100 teaching hours per year).
- She participates in examination committees.
- She has been engaged in clinical work at the **Clinic of Nuclear Medicine at University Hospital "St. Marina" – Varna** since 2015, actively collaborating with multidisciplinary teams.

Personal Impressions and Conclusion

Dr. Marina Dyankova stands out as a dedicated and highly competent specialist in the field of nuclear medicine. The presented scientific work reflects her in-depth approach, knowledge, and clinical interest in complex diagnostic cases. Noteworthy are the high quality of her analyses and her skillful interpretation of hybrid imaging studies, as well as her commitment to multidisciplinary coordination and precision—qualities that are increasingly essential in modern oncology and personalized medicine.

Ambitious, diligent, and fully devoted to her profession, Dr. Dyankova continues to contribute significantly both to the advancement of imaging diagnostics in clinical practice and to its academic establishment.

Based on the submitted:

- scientific publications with high impact factor and international citations,
- original scientific and applied contributions,
- active teaching and clinical engagement,
- personal and professional qualities,

I recommend Chief Assistant Dr. Marina Dyankova for appointment to the academic position of Associate Professor.

Varna

July 29, 2025

Assoc. Prof. Zhivka Dancheva Mezan, MD, PhD