

TO: The Chairman of the Scientific Jury, determined by Order No. R-2392/12.07.2024 of the Deputy Rector of the Medical University - Plovdiv

### **REVIEW**

Competition for the occupation of the academic position "ASSOCIATE PROFESSOR" in Medical radiology and roentgenology (including the use of radioactive isotopes) in the field of higher education "Health and Sports" by professional direction 7.1. "Medicine" at the Radiation and Nuclear Medicine Section, cat. "Clinical Oncology" for the teaching of Bulgarian and English-speaking students in medical specialty "Medical radiology and roentgenology "(incl. use of radioactive isotopes) announced for the needs of MU- Plovdiv in the State Gazette, no. 35 /19.04.24 and according to a decision for holding a competition of the Faculty assembly of the Faculty of Medicine of the MU Plovdiv (no. 7 /09.07.2024) for the occupation of the academic position "ASSOCIATE PROFESSOR" with a single candidate chief assistant Dr. Albena Dimitrova Botushanova, MD

By Prof. Dr. Elena Nikolova Piperkova, MD, PhD
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### DEAR MADAM PRESIDENT,

Pursuant to Art. 4(2) and Art. 25 of the LDASRB and Art. 2, Art. 57(2) of the Regulations for the Implementation of the LDASRB, approved proposal by the Faculty assembly of the Faculty of Medicine, MU-Plovdiv to conduct a competition and Order of Deputy Rector of MU-Plovdiv, № P-2392/12.07.2024, I have been appointed as a member of the scientific jury (SJ). At the first meeting of the SJ, I was chosen to present a peer review of the documents submitted for participation in a competition for the occupation of the academic position "ASSOCIATE PROFESSOR" in the scientific specialty "Medical radiology and roentgenology (including the use of radioactive isotopes) in the field of higher education "Health and Sports" by professional direction 7.1. "Medicine" at the Radiation and Nuclear Medicine Section, cat. "Clinical Oncology" for the teaching of Bulgarian and English-speaking students in medical specialty "Medical radiology and roentgenology "(incl. use of radioactive isotopes) announced for the needs of MU-Plovdiv in the State Gazette, no. 35/19.04.24

Analysis of the career profile of the only candidate in the competition, Assistant Professor Dr. Albena Botushanova, MD:

Dr. Albena Dimitrova Botushanova was born on 05.06.1966. She graduated from the Faculty of Medicine of the Medical University of Plovdiv in 1992 with excellent results. From 07.02.1995 she started working as a resident doctor in the Radiotherapy Clinic in the Laboratory of Radiobiology at UMBAL "St. Georgi" EAD - Plovdiv. She has acquired a medical specialty "Radiobiology" Diploma series BS No. 000033, Reg. No. 002850/06.05.1998 Since

1999, she has been working in the Department of Nuclear Medicine at the Radiotherapy Clinic and in 2003 she acquired a second specialty in Nuclear Medicine - Diploma Series Bs No. 000422, Reg No. 007872/27.01.2003. Since 2004, she has been working on the scientific topic "Nuclear medicine methods for the diagnosis of abnormal parathyroid glands in primary and secondary hyperparathyroidism" and obtained the educational and scientific degree "Doctor" in the scientific specialty "Medical radiology and roentgenology " (incl. use of radioactive isotopes) " at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Diploma Reg Nº 336/23.05.2019. Since September 2019, she has been elected as an assistant at the "Clinical Oncology" department of the MU - Plovdiv. Participates in the teaching of students of medicine and dentistry in the study discipline "Radiology". He is also a teacher at the Medical College - Plovdiv of X-ray laboratory assistants in the academic disciplines "Nuclear Medicine" and "Radiobiology".

Dr. A. Botushanova graduated as a Master in Health Management at the Higher School of Agribusiness and Regional Development, Plovdiv, Faculty of Economics and Management with Diploma Reg Nº 336/ 23.05.2019.

Since 2020, she is the head of the Department of Nuclear Medicine at the UMBAL "St. Georgi" EAD - Plovdiv, which has two bases with hybrid SPECT/CT and PET/CT gamma camera equipment. From 2021, after a competition, Dr. A. Botushanova, PhD, holds the position of "Chief Assistant" at the Department of Clinical Oncology.

During the period of her development as a doctor, university teacher and scientist with research and publication activity, Dr. Botushanova participated in postgraduate training courses, worked on scientific projects, manuals - study aids for students, participated in numerous examination and competition committees and others.

### General description of the submitted materials for the competition:

The presented by the candidate Chief assistant Dr. Albena Botushanova, PhD documents for the competition are in accordance with the requirements of the LDASRB and the Regulations for the implementation of the LDASRB in MU-Plovdiv, regarding the procedure for awarding AP "Associate Professor". All the required materials are available, informative, very well structured, which allows me to make a responsible analysis and enable me to draw definite conclusions as a member of the SJ. With Dr. Botushanova's marked hard work and modesty, and the check I made in the European periodical on nuclear medicine, I found a substantially higher Impact Factor than she indicated.

## Evaluation of the candidate's scientific works for the overall academic development:

The academic development of Dr. Albena Botushanova, PhD includes a complex assessment of scientific production and publication activity, application of her scientific and practical achievements, participation in scientific projects, educational and teaching, diagnostic and therapeutic activities and incl. personal contributions related to them.

### Analysis of the scientific-metric indicators of the candidate:

Dr. Albena Dimitrova Botushanova, PhD, participates in the current competition for the academic position "Associate professor" with a total of 22 scientific papers related to her research activity, described in folder No. 9 of the above documents. A total of 22 scientific works are presented: 1 dissertation work for obtaining the educational and scientific degree "doctor"; 1 monograph; 2 contributions to scientific aids (collections); 9 scientific articles in journals referenced in Web of Sciences and Scopus databases; in 10 referenced until 2013 and 3 until now reports with published abstracts in scientific publications, referenced and indexed in Web of Sciences with an impact factor; participation in one chapter of a collective monograph; 5 publications in non- referenced journals. Dr. Albena Botushanova is the only or first author in 6 of the scientific publications, 2nd - in 6 scientific publications and 3rd, as well as subsequent author in 10 scientific publications. The scientific metrics for the publication activity of Dr. Botushanova are characterized by a total IF=44,301 from articles (1.6) and from published summaries in referenced international journals from 2005 to the moment of this competition (43,301). Has over 20 citations in referenced in Web of Sciences and Scopus journals.

The quantitative assessment of the academic work of Dr. Albena Botushanova, PhD, according to the requirement of NACIT for the acquisition of scientific degrees and titles in her teaching and research activities, is estimated with 583 +200 points, a total of 783 points and when the citations are added, impact the factor, the qualifications and the positions held by the candidate, the total number of points is 1673.1, which exceeds the required minimum for awarding AD "Associate Professor".

### Scientific output and contributions:

- I. Particularly valuable is the contribution for the assessment and the implementation in the clinical practice the diagnosis of parathyroid gland diseases:
- Dr. A. Botushanova, PhD, successfully defended her dissertation on "Nuclear medicine methods for diagnosis of abnormal parathyroid glands in primary and secondary hyperparathyroidism":
- 1. For the first time, the results of nuclear medicine examinations performed in a large group of patients with primary and secondary hyperparathyroidism (PHPT) and (SHPT) are summarized.
- 2. The advantages and disadvantages of single-isotope two-phase modalities and two-isotope subtraction method with the addition of SPECT and SPECT/CT with 99mTc-sestamibi or 99mTc-tetrofosmin in patients with PHPT and SHPT are presented.
- 3. The role of the SPECT technique for increasing the diagnostic sensitivity of single-isotope two-phase and two-isotope subtraction methods is emphasized.
- 4. For the first time in our country, a thorough study of the relationship between a scintigraphic finding and indicators of calcium-phosphorus homeostasis, as well as with the volume of the ultrasound's finding in patients with PHPT and SHPT, has been carried out.
- 4. For the first time in the available literature, the risks of false-negative and false-positive results in the nuclear medicine diagnosis of parathyroid gland diseases have been identified and indicated.

- 5. For the first time in our country, protocols for the combined use of SPECT/CT technique with single-isotope two-phase and subtraction methods in the diagnosis of PHPT and SHPT have been prepared and implemented.
- 5. An algorithm for the examination of parathyroid glands has been prepared and put into practice

# II. A contribution to the education of medical specialists is the in-depth monographic work "Nuclear Medicine and Parathyroid Glands - Past, Present and Future".

The monographic work is a continuation of the candidate's dissertation work. It clearly highlights the personal contribution of Dr. A. Botushanova, PhD in nuclear medicine diagnostics for early, more accurate detection of parathyroid gland diseases and subsequent treatment. The author summarizes the world and Bulgarian experience in the search for the right radiopharmaceutical for the diagnosis of abnormal parathyroid glands, as well as the development of new methods in connection with technological progress in nuclear medicine equipment. Each chapter explores the past, present, and future directions of parathyroid scintigraphy research. A personal contribution can be defined as evidence material with images of own patient cases made in the Department of Nuclear Medicine at the UMBAL "St. George" EAD - Plovdiv with various radiopharmaceuticals and hybrid equipment.

# III. Scientific contributions of the publications submitted for participation in the competition

A. Publications in scientific publications, referred/indexed-Scopus Wed of Science:

- 1. Contribution of studies and case studies of the role of 18F-FDG PET/CT in different non-oncological pathology: Three of the articles consider the role of 18F-FDG PET/CT in several aspects of application in: a patient with MEN1 syndrome for detecting a parathyroid adenoma, in a patient with infectious mononucleosis (IM), in a patient with infective endocarditis, and in a patient with breast carcinoma with an incidental finding of a parathyroid adenoma (Articles 9, 10, 11, and 12)
- 1.1. Article (9) presents a case of a 47-year-old woman with multiple endocrine neoplasia type 1. 18F-FDG PET/CT revealed a low metabolically active lesion with a diameter of 10 mm (SUV max 2.00) located under the left lobe of the thyroid gland, suspicious for parathyroid adenoma. To further characterize the lesion, two months later a single-isotope biphasic 99mTc-tetrofosmin scintigraphy combined with an early SPECT technique on a SPECT gamma camera (SYMBIA E DUAL) was performed. The study visualized an area of hyperfixation located dorsally on the caudal part of the left lobe of the thyroid gland associated with a hyperfunctioning parathyroid adenoma. This case allowed us to compare two nuclear medicine techniques, with different equipment and radiopharmaceuticals PET/CT with 18F-FDG and single isotope dual- phase 99mTc-tetrofosmin scintigraphy combined with early SPECT in the same patient. Various factors may explain the different diagnostic information obtained.

- 1.2. The role of whole-body PET/CT with 18F-FDG in clinical cases with COVID-19 is indicated. The article (10) presents the case of a young patient who developed severe infectious mononucleosis (IM) caused by reactivation of EBV and CMV several months after a recent COVID-19 infection. The same is proven after a wide differential-diagnostic panel on the occasion of an unclear febrile state, severe adynamia and lack of organ symptoms. The diagnosis was also supported by a whole-body PET/CT examination with 18F-FDG, combined with low-dose CT on a hybrid PET/CT "Siemens" device, model "Biograph mCT64". 18F-FDG PET/CT is indicated for imaging infectious/inflammatory diseases, as it has been shown that cells involved in these processes are capable of expressing high levels of glucose transporters and hexokinase activity.
- 1.3. Role of 18F-FDG PET/CT in the diagnosis of infective endocarditis (IE). Article (11) presents a case of culture-negative prosthetic IE diagnosed with 18F-FDG PET/CT. Infective endocarditis is a difficult-to-diagnose disease that causes significant morbidity and mortality. A new diagnostic method, 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT), improves the diagnosis in these difficult cases. The most recent European guidelines for IE (2015) include this imaging modality as the main diagnostic criterion.
- Studies contribute to the diagnosis of breast cancer:
- An article (12) describes a case of a patient with proven breast carcinoma in which a rounded lesion suspicious for a parathyroid adenoma of the lower right parathyroid gland with mildly elevated metabolic activity, SUVmax-2.91, was visualized on hybrid PET/CT images. Ultrasound of the neck shows a solid, hypoechoic, rounded mass with a peripheral blood supply, suspicious for a lower right parathyroid adenoma. After 1 month, the patient underwent single isotope dual-phase scintigraphy with 99 mTc-tetrofosmin, combined with early SPECT/CT technique on SPECT/CT gamma camera "Siemens," model "Symbia Intevo 6". In the early phase (20 min.) and on early SPECT/CT images, an area with increased accumulation of the radiotracer suspicious for a parathyroid adenoma was visualized under the right lobe of the thyroid gland. The patient underwent surgery, in which a parathyroid adenoma was histologically proven. This case shows that PET/CT 18F-FDG can be useful for detecting the parathyroid gland.
- 3. Contributions to the diagnosis of Carcinoma of the lung is discussed in an article (7). Lung cancer is a leading cause of cancer morbidity and mortality worldwide with more than 2 million newly diagnosed cases in 2018. The disease is usually diagnosed at stage 3 or 4 with pronounced clinical symptoms, which is a poor prognostic factor. About 40% of patients with brain metastases have primary lung cancer, which indicates the importance of this pathology. The main treatment option for inoperable lesions is radiosurgery, which can be done more than once in case of progression. This enables the delivery of a high dose in a small volume with a high dose gradient while preserving healthy tissues. Re-irradiation provides a change for a good quality of life in patients with a long-life expectancy. This case confirms that double and even triple reirradiation with CyberKnife is an effective and safe therapeutic option for patients with brain metastases.
- 4. The role of SPECT/CT for the diagnosis of malignant bone lesions is discussed in article (8) Early detection of malignant bone lesions has an important role for accurate staging and optimal clinical management of malignant diseases. Proving them requires a correct choice

of imaging methods in view of optimal informativeness of the obtained results. The overview presents the different types of lesions, their characteristics with a focus on clinical practice. The advantages of the hybrid SPECT/CT technique are presented, the existing data on its application in various malignant diseases are analyzed, including the possibilities for therapeutic follow-up. Advances in technology have led to the appearance of quantitative SPECT/CT with new possibilities for applying the method in this direction.

- 5. The individualized approach in metabolic radionuclide therapy with 131-radioiodine in the postoperative period in differentiated thyroid carcinoma was evaluated. A publication (6) addressed the topic of the appropriate dose of radioactive iodine for ablation of residual thyroid parenchyma in patients operated on for differentiated thyroid carcinoma. It has been suggested that in the majority of patients with thyroid remnants after surgery for differentiated thyroid carcinoma, a single therapeutic 131I dose of 80-100 mCi is sufficient to ablate the thyroid remnants. The need for a second dose of therapeutic 131I is assessed by thorough evaluation of thyroglobulin values.
- 6. In the field of nephrology, articles (1) and (2) published results of studies of the possibilities of nuclear medicine methods in the diagnosis and follow-up of patients with chronic renal failure (CKD). In article (1), the aim is to investigate the influence of age, gender and body weight on bone changes in pre-dialysis patients with chronic renal failure (CKD). No significant difference was observed in the incidence and severity of bone changes in men and women with uremia. Bone changes are more common and pronounced in men up to the age of 40, while this trend reverses after menopause. Higher body weight was beneficial for bone changes only in women with advanced CKD, while no correlation with densitometric parameters was observed in all other patients.

Article (2) addresses the application of serum osteocalcin as a marker of bone synthesis in patients with renal osteodystrophy. A study of serum osteocalcin as a marker of bone synthesis in CKD patients in the pre-dialysis stage is recommended. Our results show that more than 50% of patients have signs of renal osteodystrophy.

B. Publications in non-referenced peer-reviewed journals or edited collective volumes: The quantitative SPECT is a new step in the development of bone scintigraphy and its application. Articles (1) and article (4) indicate the importance of semi-quantitative indicators in nuclear medicine diagnostics with SPECT and SPECT/CT for increasing their diagnostic value and possibilities for evaluating the effect of the treatment of previously described hyperactive lesions of different origin.

## Citation of the candidate's publications in the national and foreign literature

The attached citation report of Dr. Albena Botushanova, PhD shows 20 citations to one article: Yaneva, Mariana P; Botushanova, Albena D; Grigorov, Liubomir A; Kokov, Julii L; Todorova, Elena P; Krachanova, Maria G Evaluation of the immunomodulatory activity of Aronia in combination with apple pectin in patients with breast cancer undergoing postoperative radiation therapy. FOLIA Medica 2002; XLIV, vol. 1&2; yr. 22-25. ISSN 0204-8043; ISSN 1314-2143. All citations are in MBD journals in SCOPUS. Official evidentiary material is presented, in which there is citation.

### Comprehensive evaluation of the teaching-methodical and teaching activities:

Criticisms and Recommendations - I have no criticisms. Dr. Botushanova is an extremely humble worker and dedicated colleague, and I recommend more participation in Guild meetings, national and international scientific forums to transmit and share her knowledge and experience.

### Personal impressions of the candidate:

I know Dr. Albena Botushanova, PhD as a constantly developing doctor, nuclear medicine specialist for many years, as a scientific researcher and dedicated university teacher, who has reached high professionalism in the fields of clinical and scientific-theoretical clinical nuclear medicine and the most - modern hybrid metabolic imaging diagnostics of SPECT/CT and PET/CT - an important irrevocable element in earlier, more accurate diagnosis, early staging and restaging of oncological diseases for the most effective individualized treatment of patients with oncological diseases, in monitoring the effect from the antitumor therapy and the early detection of relapses, for their timely overcoming and improvement of the prognosis. Dr. Botushanova is respected and knows how to lead and work in a team. She is highly responsible and competent and has contributed to establishing a high level of diagnostic and therapeutic activity, scientific innovative and teaching academic work at MU and UMBAL "St.George", Plovdiv. Respected, preferred by his students and colleagues as a teacher and by patients as a doctor they trust. I recommend that she continue his future work in these directions by building on what has been achieved and creating new specialists and scientists under her leadership.

# General evaluation of the procedure and the candidate's compliance in the competition:

All stages of the Tender Disclosure and Announcement Procedure have been followed. They are in accordance with the requirements of the LDASRB and the "Regulations for the application of the LDASRB" in MU-Plovdiv. The only candidate in the competition, Chief Assistant Dr. Albena Botushanova PhD, meets and exceeds the minimum national requirements under Art. 2b, par. 2 and 3, respectively, to the requirements under Art. 2b, par. 5 of LDASRB and those specific to MU-Plovdiv under direction 7.1. Medicine (medical-clinical activity), defined in the "Regulations for Academic Development" at MU-Plovdiv. The scientific works presented in the competition have a marked scientific/scientific-applied character and are aimed at modern diagnostic and therapeutic problems in general medical pathology and clinical oncology. The scientific developments are filled with a very well-organized and structured research orientation, which proves permanently oriented scientific interests and has led to useful contributions and achievements. Scientific indicators, as well as the proven qualities of an erudite researcher, clinician and well-prepared teacher formulate the characteristics of chief assistant Dr. Albena Botushanova, PhD.

With the required 810 points for holding the position of Associate Professor at MU-Plovdiv, Dr. Batushanova, PhD, has secured 1,673.1 points according to the presented reference.

Conclusion: In view of the above, I believe that the only candidate in the announced competition for the academic position "Associate Professor" at MU-Plovdiv, namely Chief Assistant Dr. Albena Botushanova, PhD, meets the mandatory and specific conditions, as well as the scientometric criteria for occupation of AP "Associate Professor". I confidently give my positive assessment, vote "YES" and call on the honorable scientific jury to vote positively, for Chief. assistant Dr. Albena Botushanova, MD, for the position of "Associate professor" in "Medical radiology and roentgenology (incl. use of radioactive isotopes)" at MU-Plovdiv, area of higher education 7. Health care and sports, professional direction 7. Medicine.

26.07.2024 Sofia

Prepared by:

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