

STANDPOINT

By Assoc. Prof. Tosho Ganev MD, PhD

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Regarding: Dissertation work for the award of the scientific degree "Doctor" to Dr. Pavel Ivelinov Abushev, full-time doctoral student in the doctoral program "Urology", professional field 7.1 Medicine, enrolled by order No. R-109-29/30.01.2020.

By the order of the Rector of Medical University-Varna No. P-109-160/24.02.2023, protocol of the Faculty of Medicine No. 82/20.02.2023 and the decision of the Chairman of the Scientific Jury - Protocol No. 1, I have been appointed to present an opinion on the dissertation work of Dr. Pavel Ivelinov Abushev on "The role of multiparametric magnetic resonance imaging/ultrasound guided transrectal fusion biopsy for the diagnosis of prostate cancer".

The opinion was prepared in accordance with the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria and the Regulations for its application at the Medical University of Varna.

The dissertation contains a total of 130 pages, illustrated with 25 figures, 14 tables and 15 photographs. The bibliography includes 194 titles, of which 19 are in Cyrillic and 175 in Latin. The exposition is structured correctly, in accordance with the requirements for a scientific study, as follows:

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- Translated with www.DeepL.com/Translator (free version) Introduction – 1 page
- Literary review – 32 pages
- Purpose and objectives – 1 page
- Materials, subject and object of the research – 1 page
- Method - description, comparative analysis and specifics – 33 pages
- Results – 29 pages
- Discussion – 5 pages
- Conclusion – 1 page
- Summary – 1 page
- Scientific contributions – 1 страница
- Bibliography – 22 страници

The thesis abstract submitted to me in 39 pages is formatted according to generally accepted requirements.

1. Assessment of the topicality of the thesis, analysis of the study sample

The topic of the scientific work is dissertable, topical and of interest to urologists who are involved in the diagnosis and treatment of prostate cancer.

The dissertation begins with a literature review that is thoroughly extensive. It discusses the symptomatology of prostate cancer and the incidence of the disease worldwide and in Bulgaria. Space is given to consider the role of genetic testing for hereditary prostate cancer. The role of prostate-specific antigen and digital rectal examination as methods for screening and early detection of prostate cancer are studied in detail. New biomarkers and their potential role in the diagnostic process are discussed. Well-known imaging modalities such as ultrasound and bone scintigraphy are discussed in detail, as well as the increasing use of new imaging modalities such as MRI and PET scanner. Fine-needle aspiration biopsy with its now historical value and the now standard puncture tru-cut biopsy are described.

Chapter two contains the aim and objectives. The aim is clearly stated- to use a retrospective analysis to investigate the application of magnetic resonance imaging/ultrasound guided fusion biopsy for the diagnosis of prostate cancer. The objectives are specific and clear, and are consistent with the stated aim.

A comparative analysis between fusion biopsy and conventional ultrasound-guided systemic biopsy follows. Specifics of the transrectal and transperineal approaches are discussed. The performance of transrectal fusion biopsy is described in detail

2. Assessment of the results

- In the following third chapter the results of the study are presented. The total number of patients studied was 167. . The reason for the study was both patients with previous systemic biopsy studies with benign histological results and primary patients with elevated or progressively increasing serum PSA concentration and/or a suggestive clinical finding on digital rectal examination. All patients underwent magnetic resonance imaging within 3 months before fusion biopsy, and the MRI was performed according to a previously established protocol. A total of 79 biopsied patients had histologically proven prostate adenocarcinoma.
- A number of parameters were analyzed: age, previous biopsy examinations, total and free PSA, PSA density, gland volume, palpatory findings, PI-RADS, ratio between target and systemic samples, histological result, Gleason grade, clinical T stage, hospital stay and complications.
- An important finding in the analysis of local prostate gland status in patients with histologic outcome of prostate cancer was that as many as 34% of this group had soft-elastic gland consistency on digital rectal examination. In 25 patients, the verified tumor formations were located in the anterior and apical portions of the prostate, which are traditionally more difficult areas for transrectal needle biopsy. A significant correlation was found between the percentage of patients with histologically verified prostate adenocarcinoma and the PI-RADS class of their lesions. The dissertation results support the claim of a high negative predictive value of PI-RADS 2 lesions versus clinically significant prostate cancer. A correlation was found between high PI-RADS of biopsied

areas and histologically proven high-risk prostate cancer, demonstrating the accuracy and high diagnostic value of the study. The low percentage of patients with postprocedural febrility and signs of infection is noteworthy, as is the management of these limited cases with a standard antibiotic course.

Finally, the following conclusions are drawn for the use of fusion biopsy as a diagnostic method for histological verification of prostate cancer:

- It takes little time to perform the manipulation - 10 minutes on average.
 - A suitable method for diagnosing prostate cancer in patients with normal gland consistency on digital rectal examination.
 - Effective method even in cases of high volume prostate glands
 - Obtain real-time prostate morphology information
 - Precise marking of the suspect area and the ability to direct the needle to the suspect area with maximum accuracy
 - Reaching hard-to-reach areas located ventrally and apically.
 - Reduced false negative results reduce the necessity for repeat biopsy
- Correlation between high PI-RADS grade of detected lesions and histologically verified clinically significant prostate cancer demonstrates high diagnostic value

The doctoral candidate submitted the following scientific publications:

- a. Abushev. P. A correlation between the PI-RADS score and the pathological outcome post multiparametric magnetic resonance imaging/transrectal ultrasound fusion-guided prostate biopsy. Varna medical forum. 2023; брой 1
- b. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Робот-асистирана трансвезикална простатектомия. Уронет. 2022; брой 3, с. 69-71.
- c. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Робот-асистирана радикална простатектомия. Уронет. 2021; брой 3, с. 3-4.
- d. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Лапароскопска радикална простатектомия. Уронет. 2018; брой 2, с. 9-10.

3. Scientific contributions assessment

The contributions of the thesis have the necessary scientific and applied character and can be summarized as follows:

- The first scientific contribution concerns the analyzed diagnosis of prostate cancer including screening and early detection, genetic testing for hereditary prostate cancer, clinical diagnosis, digital rectal examination, prostate-specific antigen (PSA), biomarkers,

diagnostic ultrasound (TRUS) and magnetic resonance imaging (MRI), bone scan (scintigraphy) and PET scanner.

- The second scientific contribution is related to the presented specificity of transrectal and transperineal approach in Fusion biopsy for prostate cancer diagnosis, as well as the prepared comparative analysis between Fusion biopsy and classical transrectal ultrasound (TRUS) biopsy.
- The third scientific contribution is a study demonstrating the significant advantages of transrectal Fusion biopsy for the diagnosis of prostate cancer.
- The fourth scientific contribution is the established correlation between PI-RADS category and pathological outcome after Fusion prostate biopsy.

4. Critical notes

No substantive criticisms can be levelled at the thesis.

5. Conclusion

As a member of the scientific jury, I declare that Dr. Pavel Ivelinov Abushev may be awarded the educational and scientific degree "Doctor" for his thesis entitled "Role of multiparametric magnetic resonance imaging/ultrasound guided transrectal fusion biopsy for the diagnosis of prostate cancer".

I am confident that the other members of the scientific jury will also support my positive vote.

19.04.2023 г.

Varna

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Assoc. Prof. Tosho Ganev MD, PhD