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# ROLE OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING/ULTRASOUND GUIDED TRANSRECTAL FUSION BIOPSY FOR PROSTATE CANCER DIAGNOSTIC

**ABSTRACT**

**of a dissertation for the award of an educational and scientific degree "doctor"**

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The dissertation work was discussed at a meeting of the departmental council of the Department of Surgical Diseases of the Medical University - Varna, held on 31.01.2023. and is directed for public defense before a scientific jury.

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The dissertation contains a total of 124 pages, illustrated with 25 figures and 14 tables. The bibliography includes 194 titles.

## CONTENTS:

# I. INTRODUCTION

Prostate cancer is one of the leading malignancies worldwide. The symptomatology of prostate cancer is dependent on the tumor stage (Neykov, Dechev, 2012). Prostate cancer can be locally confined (tumor tissue is organ-confined), locally advanced (with spread (infiltration) to adjacent organs and tissues), and metastatic (in cases where it has spread to bones and lymph nodes) (Delkov et al., 2018). Missing symptomatology, as well as non-specific symptomatology, leads to late diagnosis of prostate cancer. Absence of complaints is observed in 47% of men who have proven prostate cancer, in advanced stage. The clinical manifestation of the disease is associated with lower urinary tract symptoms, erectile dysfunction, and hematuria (Merriel et al., 2018). Difficulty in diagnosis is seen due to the fact that lower urinary tract symptoms are common in benign conditions such as benign prostatic hyperplasia and prostatitis. Prostate cancer usually develops slowly and many men have no subjective complaints until the disease affects the urethra.

Risk factors for prostate cancer are hereditary, as well as increasing age and race. Prostate cancer risk is also relative to the country in which men live, as "pathological studies support the fact that geographic differences in prevalence do not stem from genetic factors, as men with the same genetic material placed in different environments create different prostate cancer risk" (Kolev, Genadiev). Prostate cancer, after lung cancer, is "the second most common cause of cancer-related death" (Kolev, Genadiev). Prostate cancer develops "most frequently in men over the age of 50" (Genadiev, Deliisky, 2009). The number of people newly diagnosed with prostate cancer in 2020 worldwide is 1.41 million, representing 7.3% of all people diagnosed with cancer. In recent years, the incidence of prostate cancer diagnoses in men under 17 years of age has been increasing, and in most cases they are diagnosed at an advanced stage and have poorer survival than middle-aged and older men. The reason for the increasing incidence is unknown. Potential contributing factors to be investigated are obesity, reduced physical activity, negative environmental influences, and exposure to various substances (Bleyer et al., 2019).

Classical transrectal ultrasound (TRUS) biopsy is the standard method used to diagnose prostate cancer when PSA levels are elevated or nodules are detected during digital rectal examination (Akyuz et al., 2020). Ultrasound imaging provides excellent guidance to the physician regarding the size and borders of the gland, but limited information regarding the internal glandular tissue and little or no details of the lesions. Diagnosis of prostate cancer using transrectal ultrasound-guided biopsy is made without visualization of the tumor site, based on anatomic characterization of the prostate gland. For many years, transrectal ultrasound (TRUS) guided biopsy has been considered as the main technique in the diagnosis of prostate cancer, by using random 12 cores to sample the entire prostate gland (Valerio et al., 2015). Conventional TRUS is commonly used for prostate cancer detection,ultrasound guided systematic biopsy and guided particle placement for radiotherapy. The main advantages of the method are related to requiring less time to perform, lower cost, and the need for equipment that is readily available. The method is primarily performed under local anesthesia (Yoon et al., 2018). The efficacy regarding the methods used for prostate cancer diagnosis is controversial. The criteria for patients to undergo prostate biopsy are either due to a persistently elevated/rising prostate specific antigen (PSA) level or abnormal digital rectal examination (DRE). Prostate biopsy may also be recommended based on pathologic results of previous biopsy studies for men found to have high-grade prostatic intraepithelial neoplasia (HG-PIN), atypical small-acinar proliferation (ASAP), etc. TRUS is defined as an inexpensive and practical tool for live imaging during procedures where the borders of the prostate and adjacent structures need to be visualized, including biopsies and brachytherapy. Magnetic resonance imaging (MRI) has high applicability as a diagnostic method in prostate cancer, from initial detection to treatment planning and disease follow-up. Functional MRI techniques, such as magnetic resonance spectroscopy, diffusion-weighted MRI, and dynamic contrast-enhanced MRI, have an increasing role in the early detection and characterization of prostate cancer. MRI allows a unique anatomical assessment of the prostate with better soft tissue resolution than any other imaging modality (Ravizzini et al., 2009). . Compared to TRUS, mpMRI has significantly better sensitivity and negative predictive

value for clinically significant prostate cancer. If used as a triage test before the first prostate biopsy, mpMRI can reduce unnecessary biopsies by one-quarter, and mpMRI can also reduce overdiagnosis of clinically insignificant prostate cancer and improve detection of clinically significant cancer (Ahmed et al., 2017).

Diagnostic methods for prostate cancer are evolving towards imaging. Advanced modes of ultrasound imaging include microdoppler, computerized transrectal ultrasound, elastography, contrast-enhanced ultrasound, and micro-ultrasound (Liu et al., 2022). Multiparametric MRI/ultrasound-guided transrectal fusion biopsy (Fusion) is increasingly being adopted due to the combined benefits of two imaging modalities and the decreasing infection rates generated by biopsy. The innovation of Fusion technology addresses key challenges associated with the standard biopsy technique, including risk of infection, patient discomfort and accurate targeting of key areas of the prostate gland. Fusion biopsy is safe, relatively convenient and highly targeted, making it an evolution in the accurate identification of prostate cancer. Fusion technology is well suited for use in difficult-to-diagnose patients with antero-apical tumors or small areas of involvement by the process, providing the opportunity for earlier histologic verification of disease. The use of Fusion biopsy allows for greater accuracy, at reduced risk to patients. The fusion biopsy procedure begins with T2-weighted, diffusion-weighted, and dynamic contrast-enhanced MRI sequences. The clarity of the MRI scan is used to:

- Resolve suspicious lesions - it is possible to exclude prostate cancer as a diagnosis based on MRI, allowing patients to avoid unnecessary biopsies.

- Obtain information needed for biopsy planning - MRI data allows identification and categorization of lesions and accurate sampling.

Fusion biopsy is cited as a major advantage with significantly improved diagnostic accuracy. In addition, the anterior and apical regions of the prostate are more easily biopsied compared to standard TRUS biopsy. Fusion biopsy is a revolutionary technology made possible by overlaying prostate ultrasound images with MRI sequences for visualization and lesion targeting. In this way, suspicious areas detected by the MRI are displayed on the ultrasound scanner, allowing the urologist to obtain the necessary biopsy materials in a targeted manner in real time.

# II. AIM AND OBJECTIVES

## 1. Aim

The aim of this clinical study is to investigate the application of Fusion biopsy in the diagnosis of prostate cancer.

## 2. Objectives

1. To analyze patients with histologic result of adenocarcinoma, including in terms of anesthesia used, PSA measured, previous prostate biopsy undergone, and digital rectal examination (DRE) results, PI-RADS category.
2. To investigate the correlation between patients with normal DRE, no symptoms and prostate cancer detected on application of transrectal Fusion biopsy.
3. To analyze the volume of the biopsied prostate, the materials collected from the patients (including the ratio between target and systemic materials), the ratio between positive and negative samples, and the comparison between ISUP grade and PIRADS score, in patients with histological result adenocarcinoma.
4. To analyze the stage of prostate cancer in patients with histological result adenocarcinoma, Gleason score and tumor location.
5. To analyze the hospital length of stay and presence of febrility in patients after Fusion biopsy was administered.

## III. MATERIALS

The materials used for the study are from the application of Fusion biopsy period 2019-2022, with 14 diagnostic procedures performed in 2019, 52 in 2020, 47 in 2021 and 54 in 2022.

## IV. RESULTS AND DISCUSSION

### 1. Analysis of preoperative data

The total number of patients studied was 167, aged between 48 and 90 years. The mean age of the patients was 65 years. In terms of percentage, the highest percentage, namely 38% of the patients were in the age range 60-69 years (Chart 1).

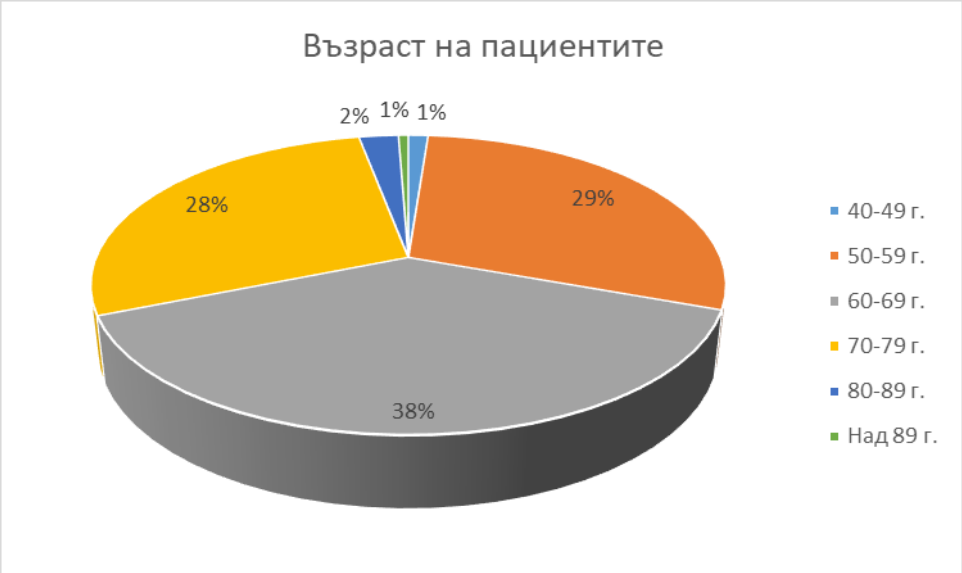


***Chart 1**: Distribution of patients by age*

Fusion biopsy was applied to patients between 2019 and 2022, with 14 diagnostic procedures performed in 2019, 52 in 2020, 47 in 2021 and 54 in 2022. The

highest percentage of prostate cancer diagnoses using Fusion biopsy was in 2022 at 32%, and it should be kept in mind that the period is until the beginning of September.

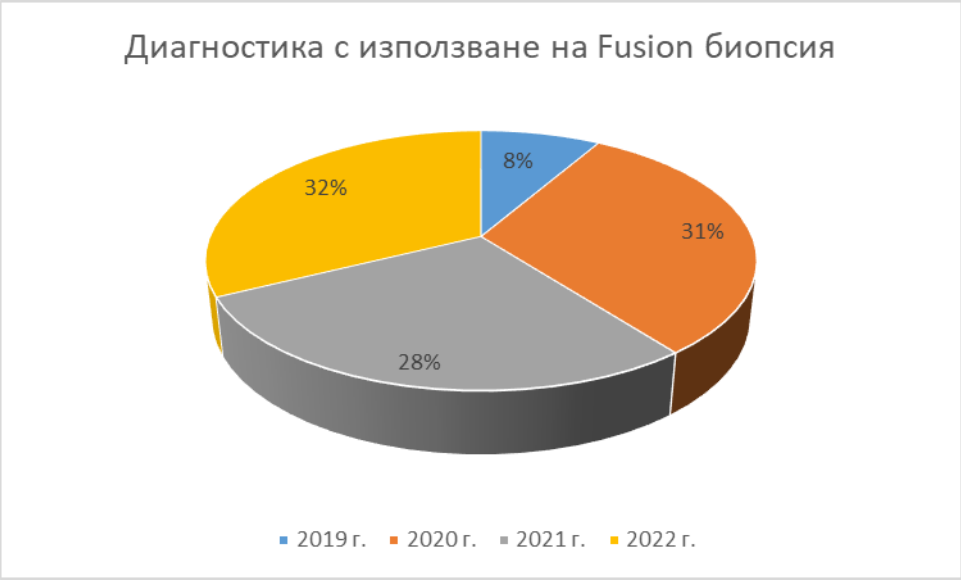


***Chart 2**: Distribution of prostate cancer diagnoses using Fusion biopsy for 2019-2020.*

## 1. Analysis of results

All patients underwent magnetic resonance imaging within 3 months before undergoing Fusion prostate biopsy. Standard protocol for MRI was T2-weighted images in at least two planes, diffusion-weighted MRI (DWI), and apparent diffusion coefficient (ADC). PI-RADS data were available for 158 of the patients, and it was found that lesions were assessed as PI-RADS 2 in 35 of the patients (22%), PI-RADS 3 in 64 of the patients (41%), PI-RADS 4 in 35 of the patients (22%), and PI-RADS 5 in 24 of the patients (15%).

Intravenous anesthesia was used in 120 of the patients (72% of all patients) and local anesthesia was used in the remaining 47 patients (28%). A total of 44 patients had undergone a previous prostate biopsy, and one patient underwent transurethral resection of the prostate (TURP). 70.45% of the studied patients underwent 1 previous prostate biopsy, 20.45% underwent 2 previous prostate biopsies and 9.09% underwent 3 previous prostate biopsies (Table 1).

***Table 1***. *Patients' previous prostate biopsies*

| Previous prostate biopsies | Number of patients | % relation to all patients with previous prostate biopsies |
|---|---|---|
| 1 previous prostate biopsy | 31 | 70,45% |
| 2 previous prostate biopsies | 9 | 20,45% |
| 3 previous prostate biopsies | 4 | 9,09% |

The histological results of the previous prostate biopsies of the patients were: BPH - 43 patients; no prostate tissue - 1 patient. Analyzing the patients with histological result adenocarcinoma from Fusion biopsy, it was found that:

- 30 patients (34%) had a histological result of BPH from one previous systemic biopsy.

- 10 patients had more than one previous prostate biopsy, and 7 of them (23% of patients with adenocarcinoma who had a histological result BPH from a previous systemic biopsy) had 2 previous prostate biopsies and 3 of them (10%) had 3 previous prostate biopsies (Chart 3).


***Chart 3:*** *Number of previous prostate biopsies, in patients with adenocarcinoma from Fusion biopsy who had a benign histological result from a previous systemic biopsy*

In 27 of the patients with verified prostate cancer (34%), the prostate gland on digital rectal examination had a soft-elastic consistency, without the presence of dense nodules and without clinical evidence of cancer. Analyzing how many of the patients with normal DRE had prostate cancer, the following results were found:

- 26 patients with normal palpatory findings were found to have adenocarcinoma.

- In one patient, the histologic result was STUMP (stromal epithelial tumor with unclear malignant potential).

The conclusion that can be reached after analysis of the above data is that even in patients with normal DRE and no symptoms, Fusion biopsy is a reliable diagnostic method for histological verification of prostate cancer (Chart 4).

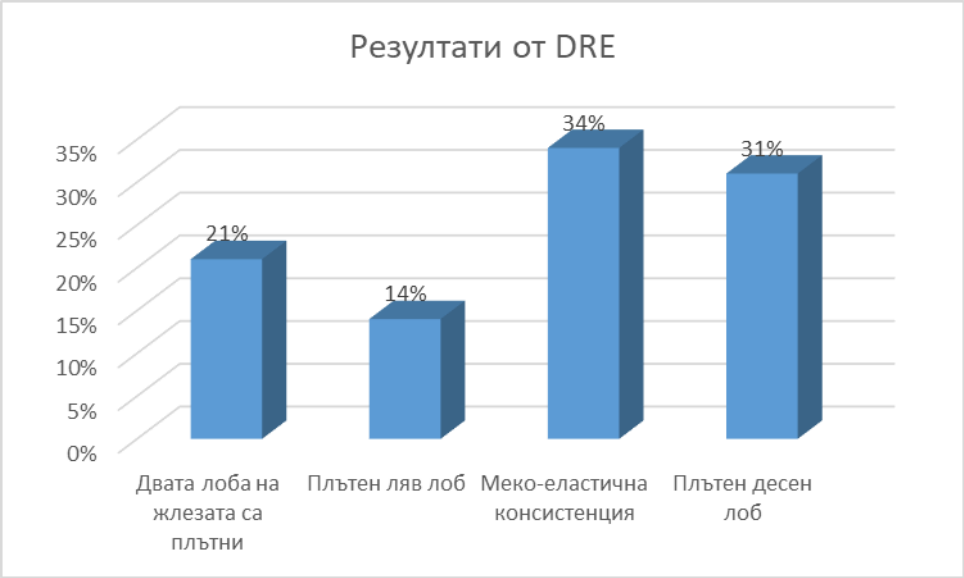


***Chart 4.*** *DRE results in the group of the prostate cancer patients*

Regarding the volume of the prostate glands in the examined patients, the following was found:

- Mean volume - 70,32 ml.

- The largest volume of the biopsied prostate - 236 ml.

- The smallest volume of biopsied prostate - 19 ml.

The size of the gland in the patients ranged from 32/37/47mm. to 83/63/67mm. The conclusion that can be reached is that even in glands with large volume, Fusion biopsy is an effective method for the diagnosis of prostate cancer.

The analysis of the material taken from all patients shows that:

- The average number of materials taken was 13.

- The most materials taken were 30.

- The least materials taken were 6.

The total materials taken from the patients were 1927, out of which:

- Target materials were 1429 (74% of all materials taken).

- Systemic materials were 498 (26% of all materials collected).

The proportion of target and systemic materials in patients is presented in the following chart 5.

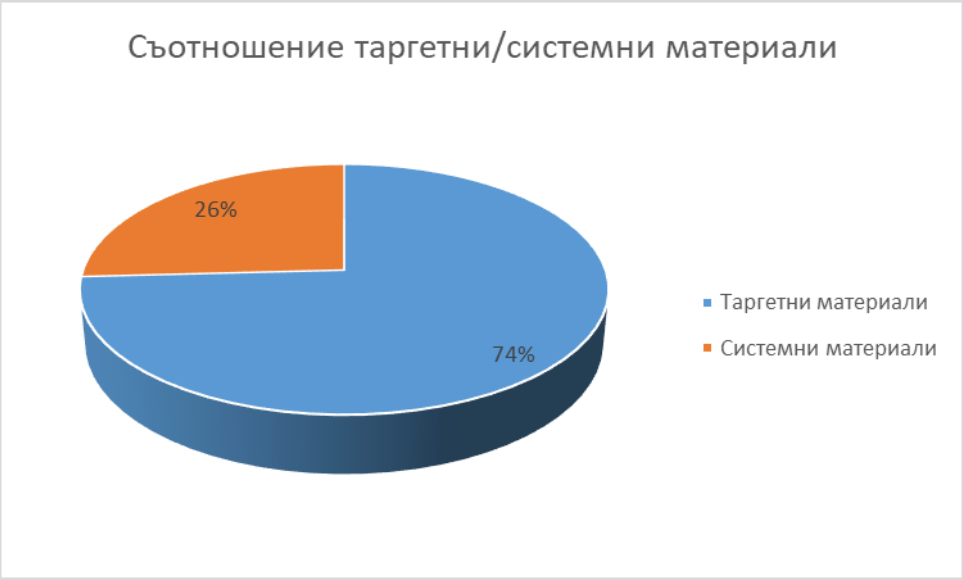


***Chart 5:*** *Ratio between target and systemic materials in patients*

The histological results of the patients are presented in Table 2.

***Table 2.*** *Histological results*

| **Хистологичен резултат** | **Брой пациенти** | **% от пациентите** |
|---|---|---|
| Acinar adenocarcinoma | 5 | 3% |
| Adenocarcinoma | 68 | 48% |
| Adenocarcinoma with extraprostatic extension | 2 | 1% |
| BPH | 36 | 22% |
| BPH, ASAP | 1 | 1% |
| BPH, chronic prostatitis | 37 | 22% |
| ДПХ, chronic prostatitis, PIN | 5 | 3% |
| Ductal adenocarcinoma | 1 | 1% |
| Foamy cell adenocarcinoma | 1 | 1% |
| Mucinous adenocarcinoma | 1 | 1% |

| | | |
|---|---|---|
| STUMP (stromal epithelial tumor with unknown malignant potential) | 1 | 1% |

The data found that:

- 87 patients had a BPH score (52% of all patients).

- 79 patients had an adenocarcinoma result (47% of all patients).

- 1 patient had a STUMP result (1% of all patients).

Data regarding the measured prostate-specific antigen (PSA) in patients are presented in the following table

***Table 3.*** *Measured PSA in patients*

| **PSA** | **ng/ml** |
|---|---|
| Highest PSA | 1,39 |
| Lowest PSA | 159,80 |
| Median PSA | 12,69 |
| Lowest Free/Total PSA | 2,7% |
| Highest Free/Total PSA | 33% |
| Median Free/Total PSA | 12,75% |

According to the data presented in table 3, the lowest measured PSA, in biopsied patients, was 1.39 ng/ml and the highest was 159.80 ng/ml, with a mean PSA of 12.69 ng/ml. In terms of Free/Total PSA, the lowest measured value was 2.7%, the highest 33%, and the mean Free/Total PSA in the patients was 12.75%.

The following PSA values were found in patients with histological result of BPH as follows:

- Mean PSA - 9.13 ng/ml.

- Highest PSA - 26.00 ng/ml.

- Lowest PSA - 3.90 ng/ml.

In patients with histological result of BPH and chronic prostatitis, PSA values were:

- Mean PSA - 9.55 ng/ml.

- Highest PSA - 26,00 ng/ml.

- Lowest PSA - 1.39 ng/ml.

In patients with histological result adenocarcinoma, PSA values were:

- Mean PSA - 15.39 ng/ml.

- Highest PSA - 159.80 ng/ml

- Lowest PSA - 3.33 ng/ml.

The graphical representation of the results in terms of lowest, highest and mean PSA, in patients with histological result of BPH, BPH and chronic prostatitis and adenocarcinoma, are presented in charts 6, 7 and 8.

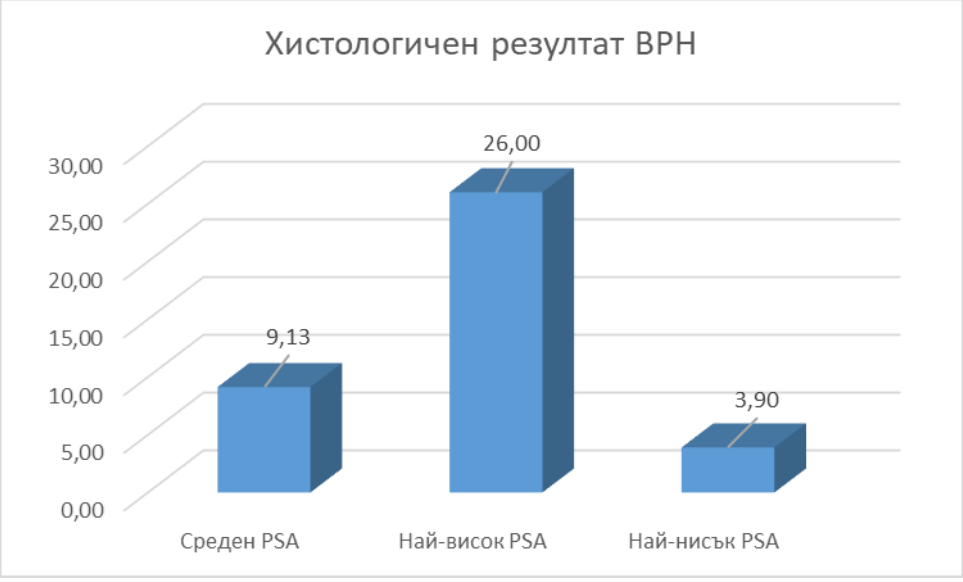


***Chart 6:*** *PSA in histological result of BPH*

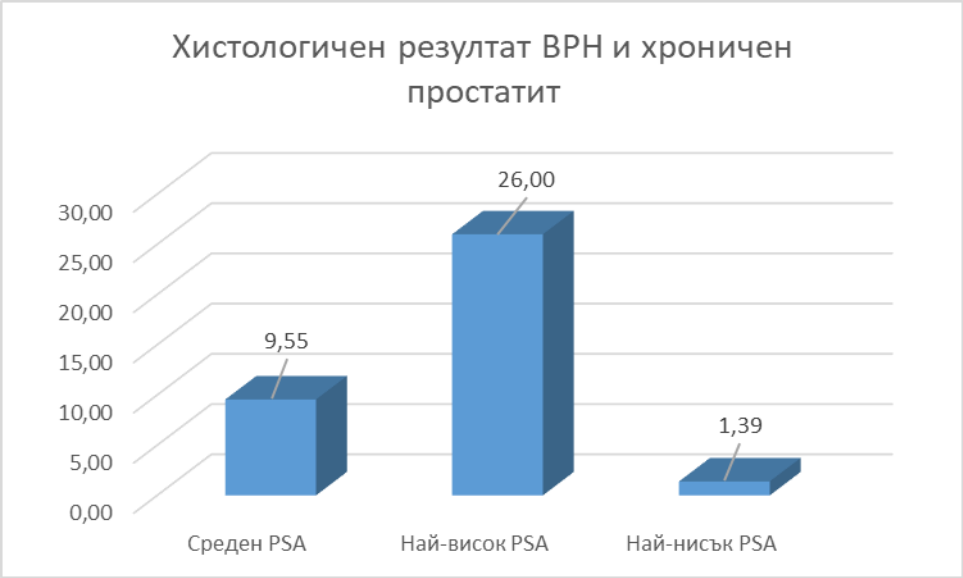


***Chart 7**: PSA in histological result of BPH and chronic prostatitis*

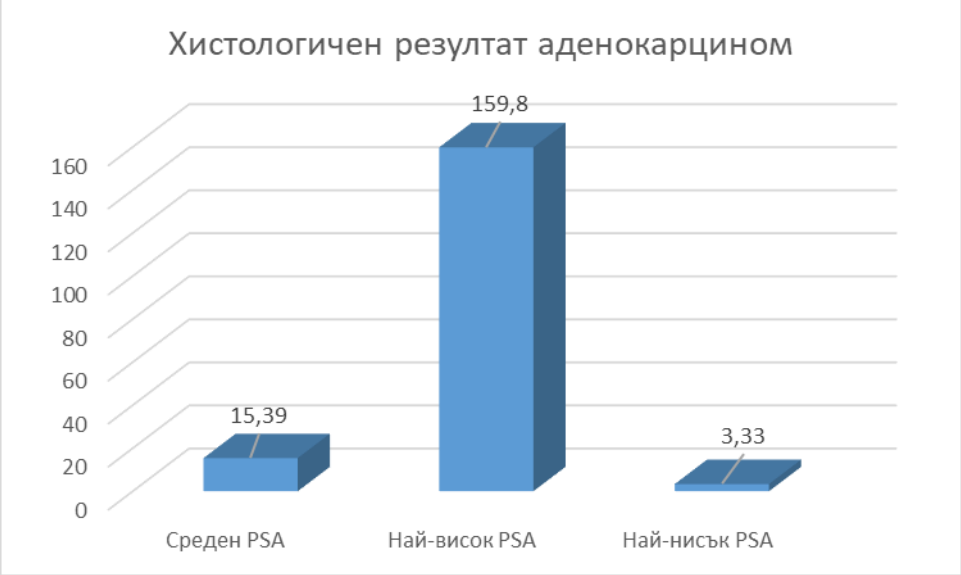


***Chart 8:** PSA in histological result of adenocarcinoma*

Patient data showed a correlation between measured PSA and histological prostate cancer score. The mean detected Free/Total PSA in patients with BPH was 13.93% and in patients with adenocarcinoma was 11.25%. The data are presented in chart 9.

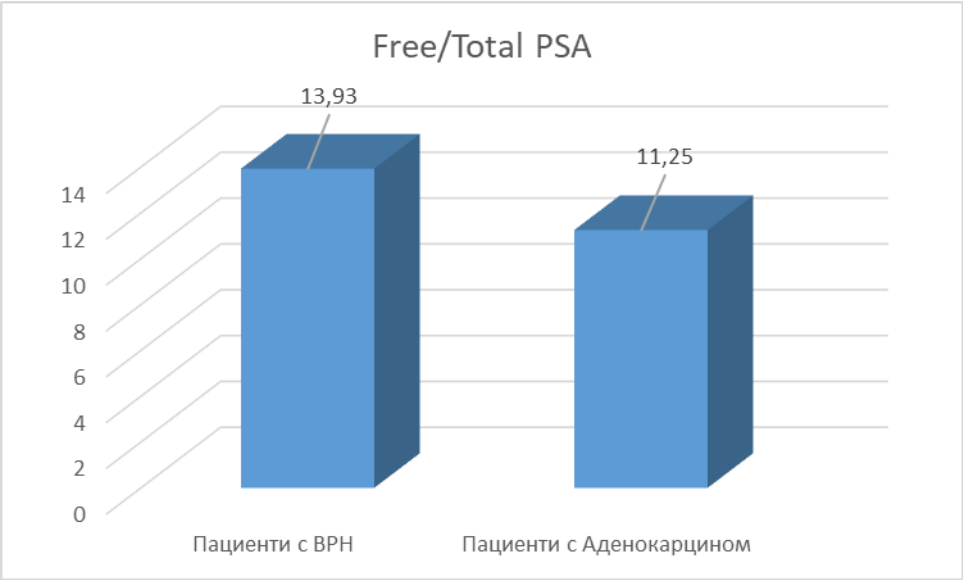


**Chart 9**. Mean Free/Total PSA in patients with BPH and in patients with adenocarcinoma

In patients with histological result adenocarcinoma is found:

- Total samples taken were 981.

- The least samples taken per patient were 6.

- The most samples taken per patient were 22.

- The average number of samples taken per patient was 12.

- Total positive samples for adenocarcinoma were 304.

- The average number of positive samples was 5.

- Positive samples for adenocarcinoma were 31% of all samples (304 samples).

- Negative samples for adenocarcinoma were 69% of all samples (677 units).

The ratio of positive to negative samples was 31:69. The data are summarised in the following table 4.

***Table 4.*** *Sample results in patients with histological result adenocarcinoma*

| Results | Number of cores | Percent |
|---|---|---|
| Positive samples | 304 | 31% |
| Negative samples | 677 | 69% |
| Total amount of cores taken | 981 | 100% |

Of all 79 patients with a histological result of BPH, 6 patients had atypical small acinar proliferation (ASAP) and 11 patients had prostatic intraepithelial neoplasia (High grade PIN). The percentage ratio is presented in the following chart 10.

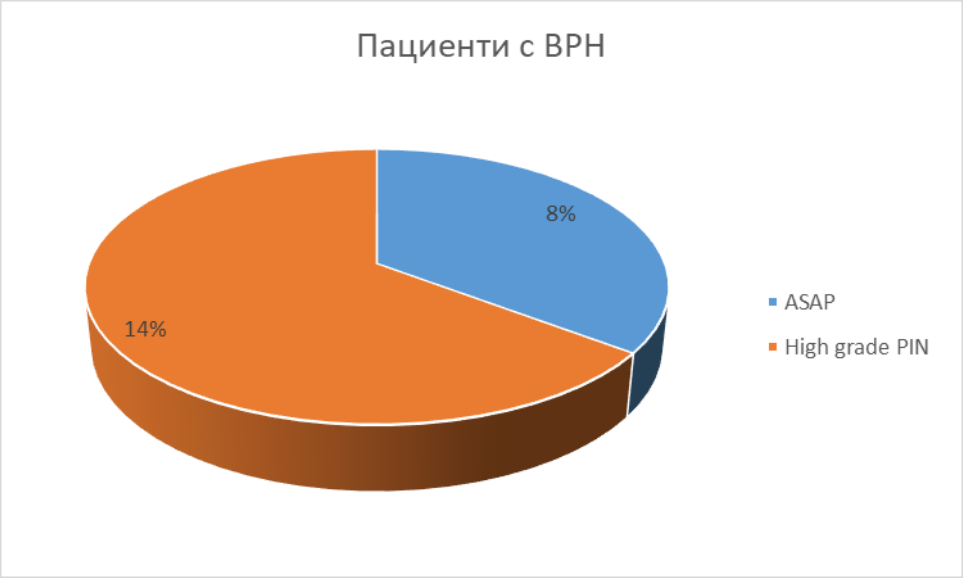


***Chart 10.*** *Proportion of patients with ASAP and patients with High grade PIN, compared to all patients with histological result BPH*

Data on staging in patients show that:

- 35% of patients had T1c prostate cancer, i.e. tumor proven after biopsy due to elevated PSA, without palpatory findings from DRE

- 18% of patients were stage T2a - tumour involving half the lobe or less.

- T2b was diagnosed in 23% of patients, i.e. the tumour in these patients involved more than half the lobe but not both lobes.

- 23% of patients had T2c - the tumour covered both lobes.

- 2% of the patients had T3a, with unilateral or bilateral tumor through the capsule.

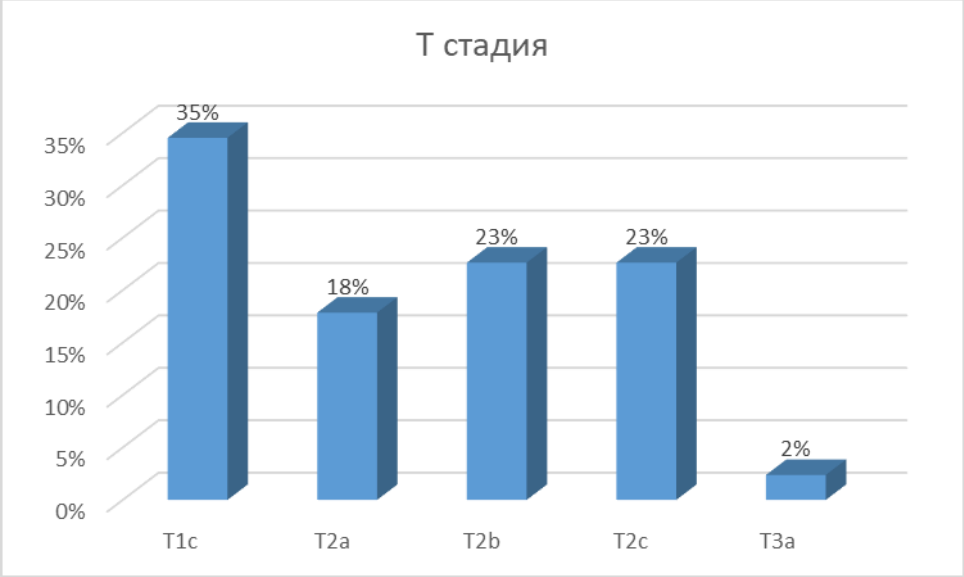


***Chart 11.*** *Proportion of T stage relative to all patients with adenocarcinoma*

Depending on the Gleason score, the distribution of patients with histological score adenocarcinoma is presented in the following table.

***Table 5.*** *Gleason score of patients with adenocarcinoma*

| Risk | Groups (ISUP) | Gleason score | Patients | % of adenocarcinoma patients |
|---|---|---|---|---|
| **Low risk** | Group 1 | Gleason score 6 | 23 | 26% |
| **Intermediate risk** | Group 2 | Gleason score 7 (3+4) | 25 | 29% |
| | Group 3 | Gleason score 7 (4+3) | 9 | 10% |
| **High risk** | Group 4 | Gleason score 8 | 19 | 22% |
| | Group | Gleason score 9-10 | 11 | 13% |

Gleason score in patients shows that:

- Low risk is found in 26% of patients with histological score adenocarcinoma. In these patients, although the tumour is unlikely to spread to other organs and tissues, surgical treatment or active surveillance should be performed after an informed patient decision.

- Intermediate risk is found in 39% of patients overall.

- High risk is found in 35% of patients.

PI-RADS data were available for 158 of the patients, finding that:

- PI-RADS 2 in 35 of the patients (22%).

- PI-RADS 3 were 64 of the patients (41%).

- PI-RADS 4 were 35 of the patients (22%).

- PI-RADS 5 were 24 of the patients (15%).

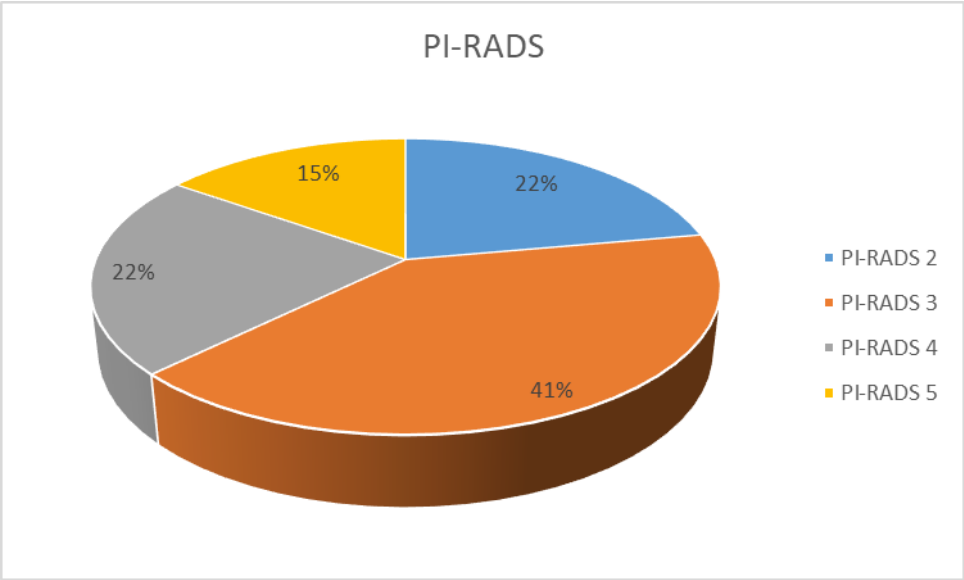


***Chart 12.*** *PI-RADS data in the patients*

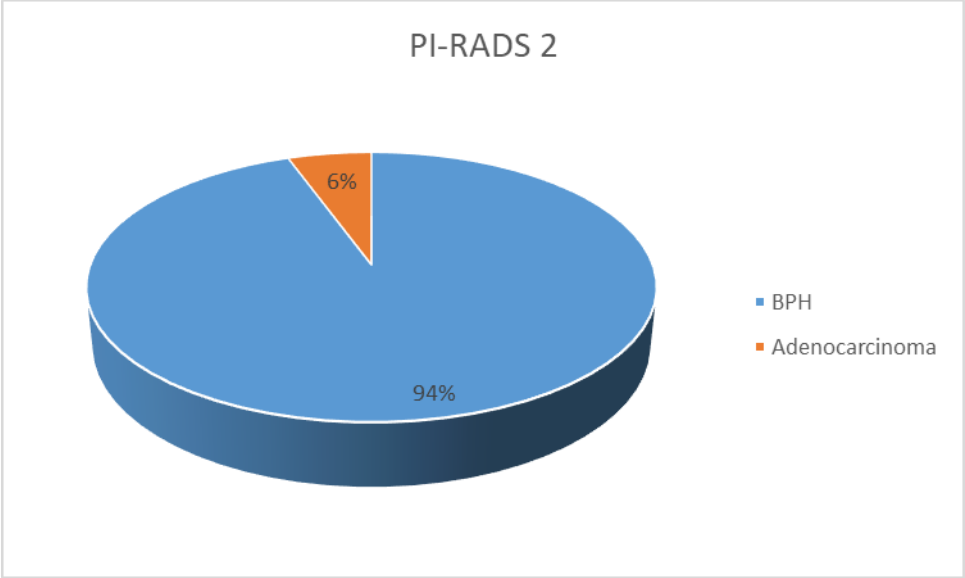


***Chart 13*** *Histology result in PI-RADS 2 patients: BPH and prostate cancer*

The data in chart 13 show that 33 (94%) of the PI-RADS 2 patients (35 in total) had a histologic result of DPH and the remaining 2 (6%) had adenocarcinoma.

PI-RADS 3 patients (64 total) were found to have:

- 38 patients (59%) had a histological result of BPH.

- With histological result adenocarcinoma were 26 patients (41%).

The data is presented in chart 14.

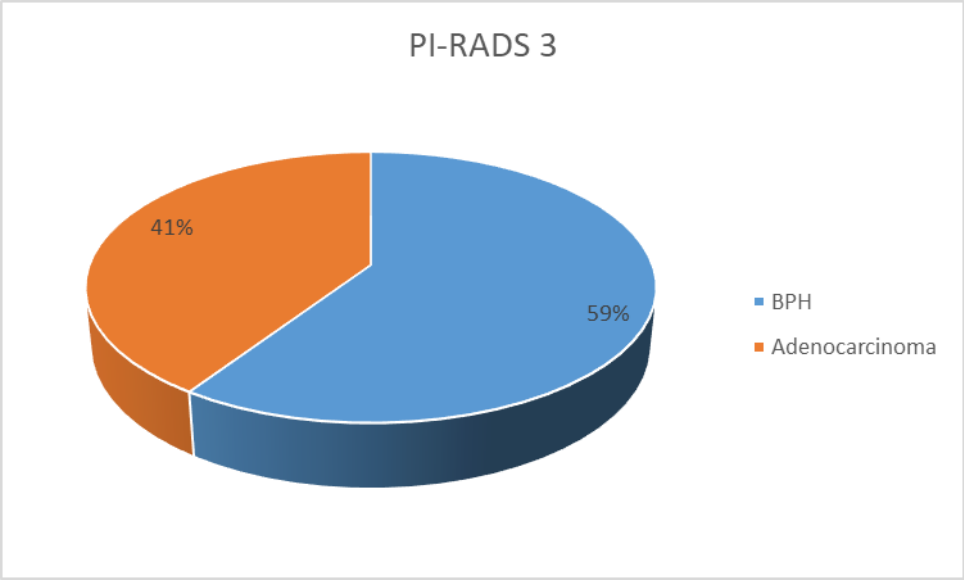


***Chart 14*** *Histology result in PI-RADS 3 patients: BPH and prostate cancer*

Of the 35 patients with PI-RADS 4 (Chart 15):

- 5 patients (14%) had a histological result of BPH.

- With histological result adenocarcinoma were 30 of the patients (86%).

Of the 24 patients with PI-RADS 5 (Chart 16):

- 1 of the patients (4%) had a histological result of DPH.

- With histological result adenocarcinoma were 23 of the patients (96%).

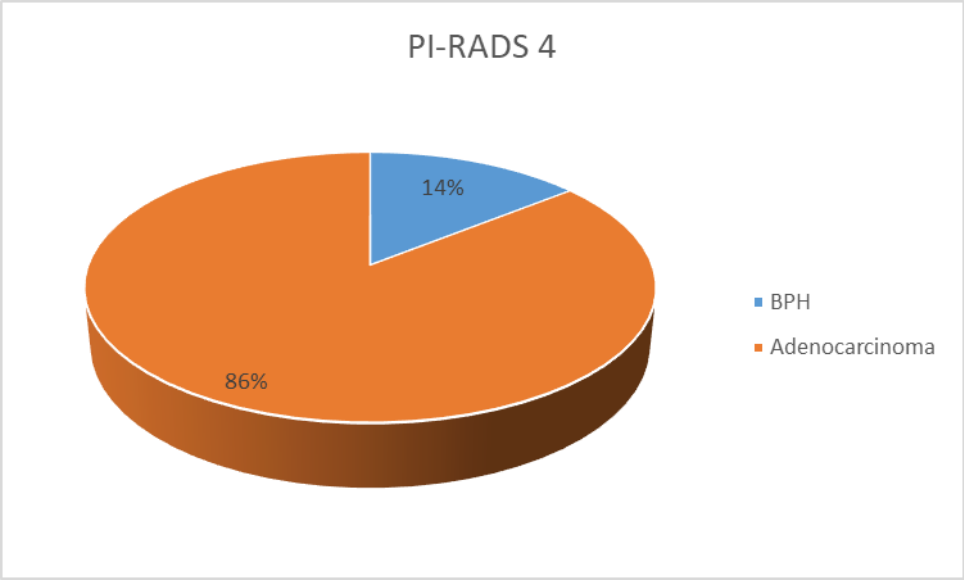


***Chart 15.*** *Histology result in PI-RADS 4 patients: BPH and prostate cancer*

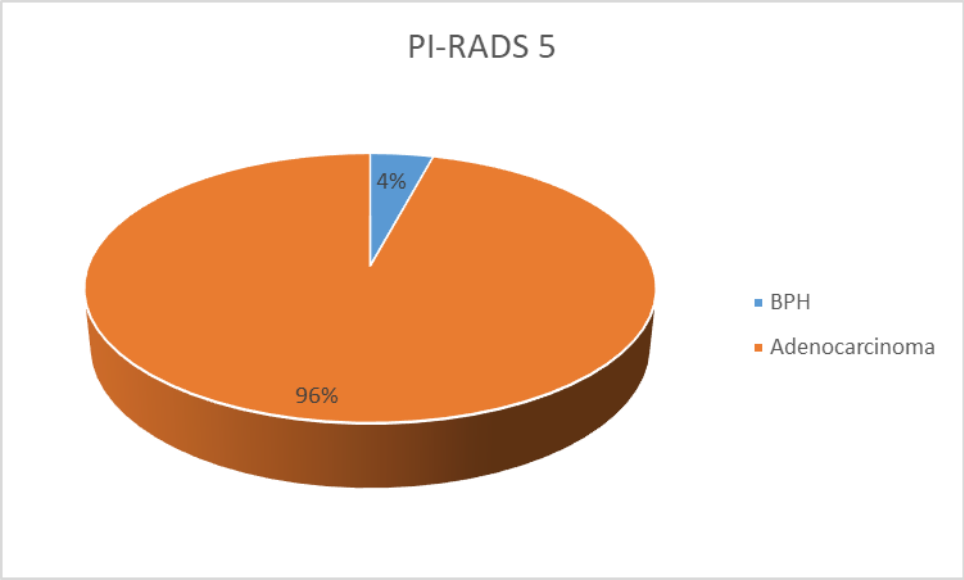


***Chart 16.*** *Histology result in PI-RADS 5 patients: BPH and prostate cancer*

In summary, the histological outcome data of BPH and adenocarcinoma in patients with PI-RADS 2, PI-RADS 3, PI-RADS 4 and PI-RADS 5 are presented in the following Table 6.

***Table 6.*** *Histology result data in patients with PI-RADS 2, PI-RADS 3, PI-RADS 4 and PI-RADS 5 lesions*

| PI-RADS | Histology result | Patients | Percent |
|---|---|---|---|
| **PI-RADS 2** | BPH | 33 | 94% |
| | Adenocarcinoma | 2 | 6% |
| **PI-RADS 3** | BPH | 38 | 59% |
| | Adenocarcinoma | 26 | 41% |
| **PI-RADS 4** | BPH | 5 | 14% |
| | Adenocarcinoma | 30 | 86% |
| **PI-RADS 5** | BPH | 1 | 4% |
| | Adenocarcinoma | 23 | 96% |

Correlation between high RI-RADS and high ISUP grade:

- In the two patients with PI-RADS 2, the ISUP grade was 1.

- In a total of 26 patients with PI-RADS 3, ISUP grade 1 was found in 12 patients, ISUP grade 2 in 10 patients, ISUP grade 3 in 3 patients, ISUP grade 4 was not found, and ISUP grade 5 was found in 1 patient.

- In a total of 30 patients with PI-RADS 4, ISUP grade 1 was found in 5 patients, ISUP grade 2 in 9 patients, ISUP grade 3 in 4 patients, ISUP grade 4 in 9 patients, and ISUP grade 5 in 3 patients.

- A total of 23 patients with PI-RADS 5 were found to have ISUP grade 1 in 2 patients, ISUP grade 2 in 6 patients, ISUP grade 3 in 1 patient, ISUP grade 4 in 9 patients, and ISUP grade 5 in 5 patients.

The comparison between ISUP grade and PIRADS score in patients with adenocarcinoma histological score is presented in the following chart 17.

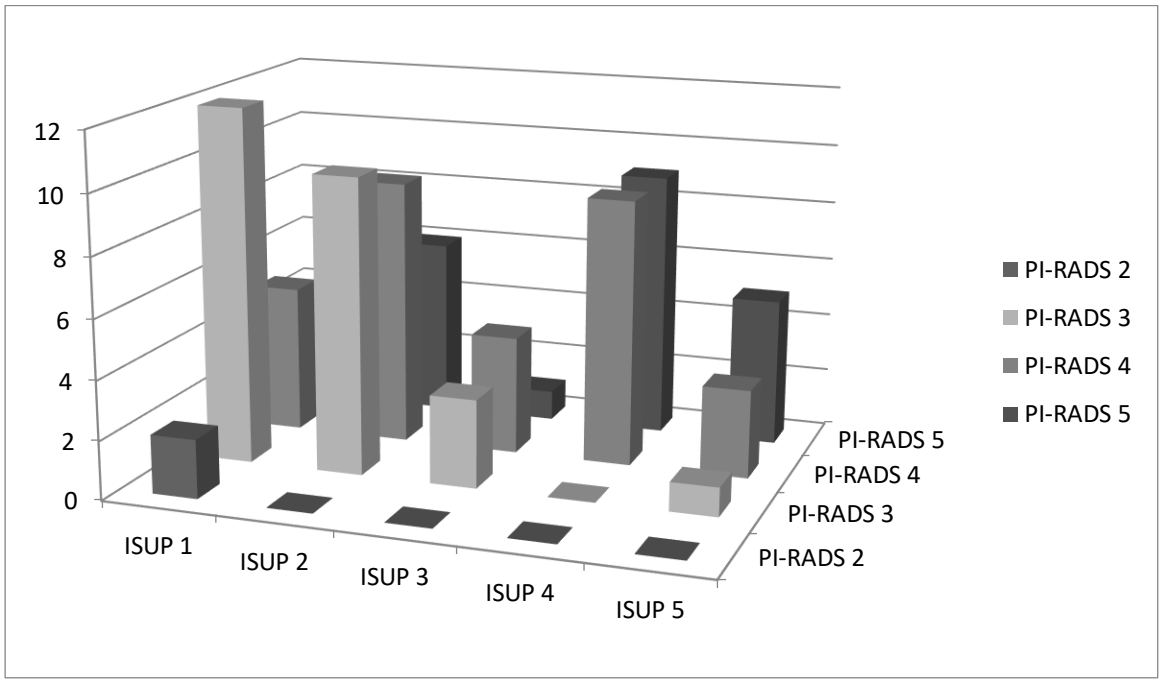


***Chart 17.*** *Relation between PI-RADS score of the MRI lesions and ISUP grade in the adenocarcinoma patient group*

Significant correlation was found between the percentage of patients with histologically verified prostate adenocarcinoma and PI-RADS class. A correlation was also found between PI-RADS 4 and PI-RADS 5 grades, and clinically significant prostate cancer (ISUP≥2). ISUP 4 and ISUP 5 were almost exclusively observed in patients with PI-RADS 4 and PI-RADS 5 areas. The only exception was one patient with an ISUP 5 histologic result in a MRI susceptible area classified as PI-RADS 3.

The tumor location in the patients (80 in total for whom data are available) is as follows:

- apex - 12 patients.
- apex, middle third - 8 patients.
- base - 12 patients.
- base, apex - 1 patient.
- base, middle third - 9 patients.
- middle third - 32 patients.
- middle third, apex - 4 patients.
- middle third, base - 2 patients.

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. The percentage of tumor location in the patients is visualized in the following chart 18.

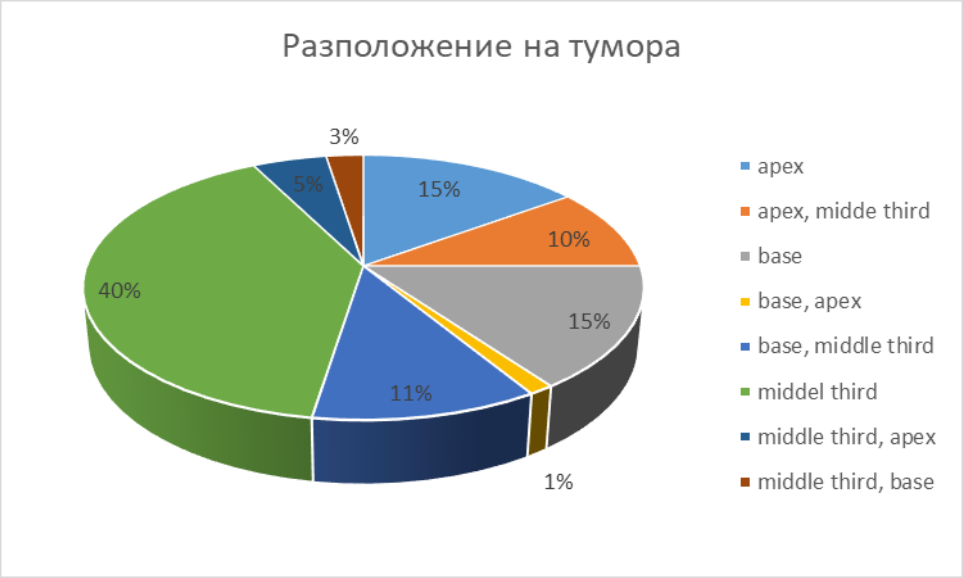


***Chart 18.*** *Location of the tumor inside the prostate gland*

Of all patients with prostate cancer, perineural invasion was found in a total of 20 (23% of patients), with:

- left side - 5 patients (25% of patients with perineural invasion).

- right side - 6 patients (30% of patients with perineural invasion).

- Bilateral - 4 patients (20% of patients with perineural invasion).

- unspecified - 5 of the patients (25% of the patients with perineural invasion).

The hospital stay of the patients was between 1 and 6 days, with an average of 2 days. Hospital stay data were available for 120 of the patients studied and are presented in the following table 8.

***Table 8.*** *Patient hospital stay*

| Hospital stay | Patients | Percent |
|---|---|---|
| 1 day | 2 | 2% |
| 2 days | 90 | 75% |
| 3 days | 18 | 15% |
| 4 days | 6 | 5% |
| 5 days | 2 | 2% |
| 6 days | 2 | 2% |

As can be seen from the data in Table 8, the largest percentage of patients (75%) had a hospital stay of 2 days (Chart 19).

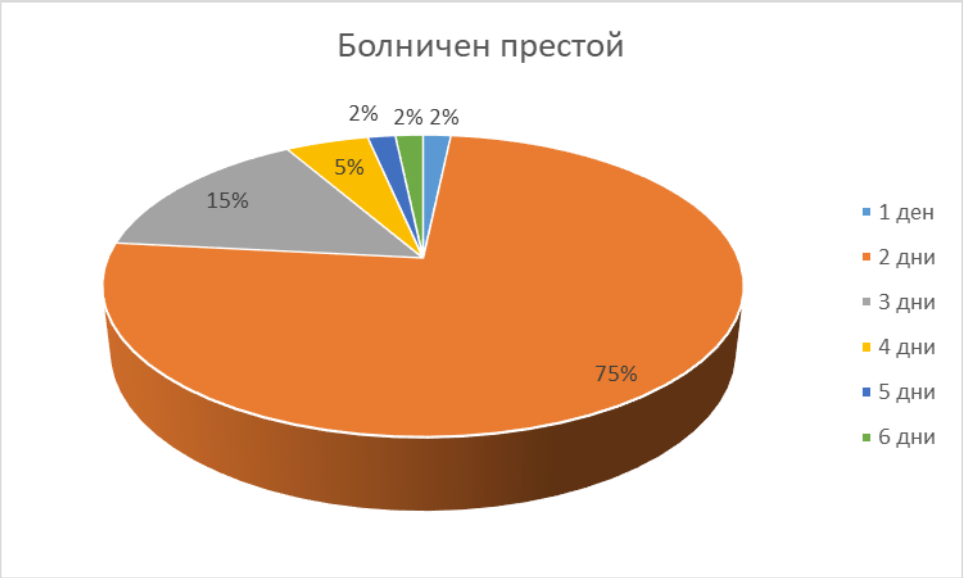


***Chart 19.*** *Graphical representation of the daily stay of patients who underwent Fusion biopsy*

Febrility after the application of Fusion biopsy was found in only four patients, or 2% of all patients. Temperature spikes did not last more than two days, and the infection was controlled with a standard course of treatment with antibiotics from the quinolone group.

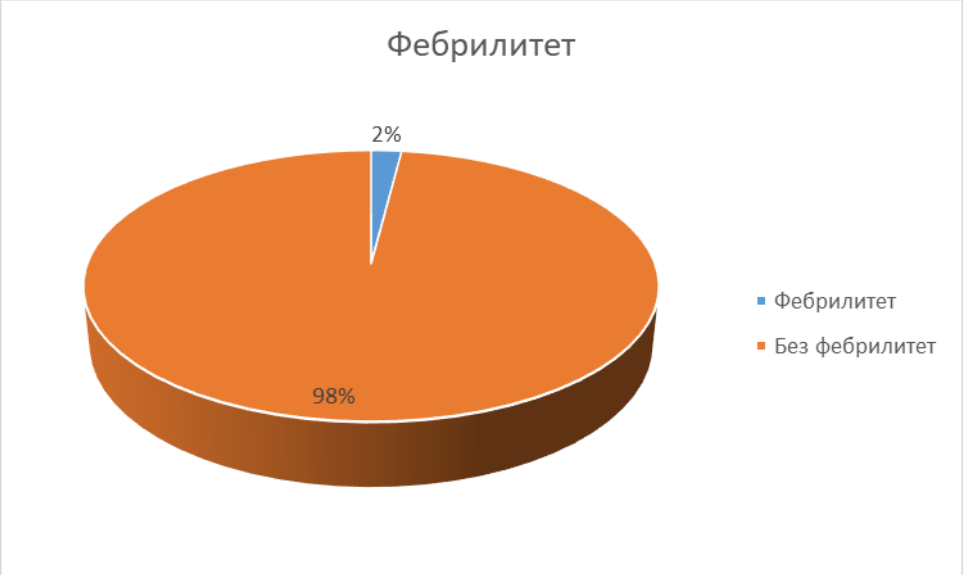


***Chart 20.*** *Febrile patients after Fusion biopsy*

The biopsied lesions in the patients were:

- The largest size - 53 mm.

- Smallest size - 4 mm.

- Medium size - 14 mm.

Biopsied lesions ranged from 4 to 53 mm, with an average size of 14 mm.

# V. SUMMARY AND CONCLUSIONS

The use of transrectal Fusion biopsy for the diagnosis of prostate cancer has its significant advantages, namely, even in patients with normal digital rectal examination, Fusion biopsy effectively diagnoses prostate cancer; works effectively even in glands with large volume; results in low rates of febrility and septicemia in patients, minimizing false negative results, etc.

Conclusions - The application of transrectal Fusion biopsy is found to:

- Accurate marking of the specimen.

- Ability to guide the needle to the suspicious area with maximum accuracy.

- Suitable method for diagnosing prostate cancer in patients with normal gland consistency on digital rectal examination.

- Effective diagnostic method even in large volume glands.

- Reaching hard-to-reach areas located ventrally and apically.

- Reduced false negative results reduce the need for repeat biopsy.

- Correlation between high RI-RADS grade of lesions detected and histologically verified clinically significant prostate cancer demonstrates high diagnostic value.

- Little time is required for the manipulation - 10 minutes on average.

- A small number of patients presented with febrility after biopsy, and in all of them febrility and infection were controlled within two days with a standard course of antibiotics with fluoroquinolones.

- Average hospital stay of 2 days.

# VI. CONCLUSION

Prostate cancer is one of the leading malignant cancers worldwide. Prostate cancer can be locally confined (tumor tissue is organ limited), locally advanced (with spread (infiltration) to adjacent organs and tissues) and metastatic (in cases where it has spread to bone and lymph nodes). Missing symptomatology as well as non-specific symptomatology lead to late diagnosis of prostate cancer. Absence of complaints is seen in 47% of men who have proven prostate cancer, in the advanced stage. Symptoms in patients are seen after the onset of urinary problems. Prostate cancer usually develops slowly and many men have no subjective complaints.

The technology used to perform a fusion biopsy combines the technologies used by transrectal ultrasonography and magnetic resonance imaging. The ability of the fusion biopsy technology to take histological material on a patient-by-patient basis from the specimens provides a greater opportunity to detect prostate cancer. Fusion biopsy is an appropriate method for detecting prostate cancer in patients who have high PSA tumor marker levels, as well as in patients with high PI-RADS stage from MRI. The method provides rapid recovery and the risk of infection is minimal. The method provides the possibility of histological verification of tumors, regardless of their localization in the prostate. Fusion biopsy is a precise and safe method for the diagnosis of prostate cancer. The correlation between a high RI-RADS grade of detected lesions and histologically verified clinically significant prostate cancer demonstrates high diagnostic value. The method is suitable both for repeat biopsy examination after previous negative systemic biopsies and for initial prostate biopsy, especially for lesions that are not palpable on digital examination, e.g. lesions located in the anterior and apical part of the gland.

# VII. SCIENTIFIC CONTRIBUTIONS

The thesis has several scientific contributions:
- 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 the transrectal and transperineal approach of Fusion biopsy for the diagnosis of prostate cancer, and the comparative analysis between Fusion biopsy and classical transrectal ultrasound (TRUS) biopsy.

- The third scientific contribution is the study conducted 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.

# VIII. SCIENTIFIC PUBLICATIONS

1. 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

2. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Робот-асистирана трансвезикална простатектомия. Уронет. 2022; брой 3, с. 69-71.

3. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Робот-асистирана радикална простатектомия. Уронет. 2021; брой 3, с. 3-4.

4. Д. Анакиевски, Р. Маринов, И. Гочева, В. Николов, П. Абушев. Лапароскопска радикална простатектомия. Уронет. 2018; брой 2, с. 9-10.