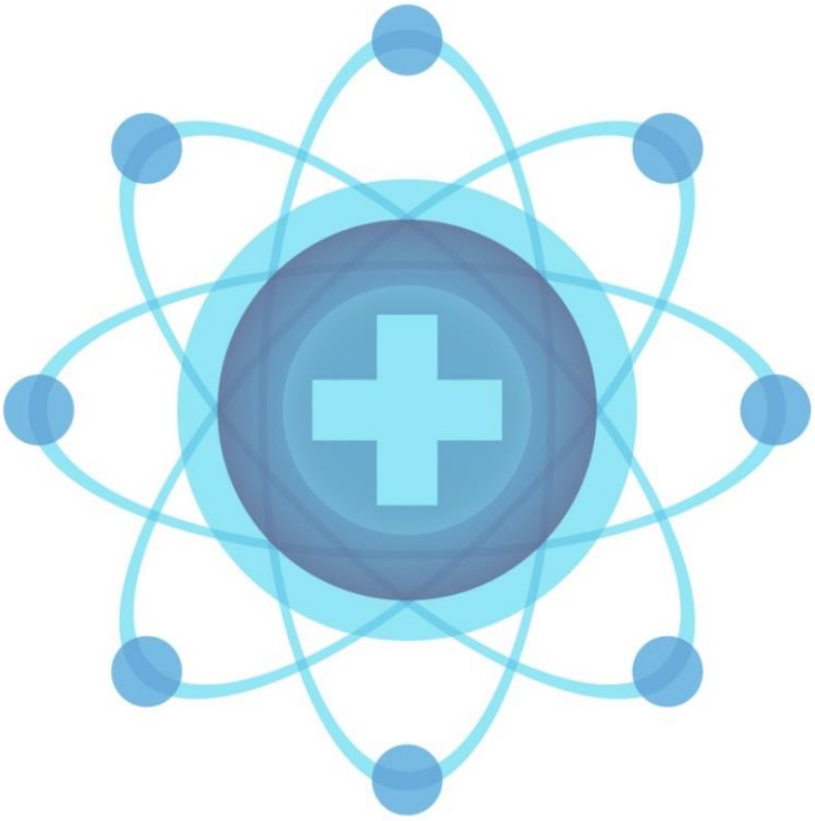

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On the issue of the significance of methods of diagnosis of prostate cancer.

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Purpose of the study. Assess the sensitivity, specificity and accuracy of the applied methods for diagnosing prostate cancer.

Material and methods. The material of the study was a group of men in the amount of 156 men examined in the period from 2020 to 2021, who were examined at the urological department of the RSSPMCOR

Results. All our patients complained of urination disorders. Due to the combination of several symptoms of urination disorders (SUD) in the overwhelming number of patients, the sum of clinical manifestations exceeds the total number of examined in this group, the leading SUD were stranguria – 95 (79.17%) patients, nocturia – 77 (64.17%) and difficulty urinating – 68 (56.67%) patients. The sensitivity of the TRUS, coupled with ultrasound angiography, was determined by us at 90%, specificity – 87% and accuracy – 89%.

Conclusion. The combination of ultrasound and ultrasound angiography makes it possible to more fully assess the stage of the tumor and predict, with a certain degree of probability, the reaction of cancer to conservative treatment, which is very important for practical oncology as a method of dynamic control of prostate cancer therapy.

Keywords: prostate cancer, significance of diagnostic methods.

Introduction. With the increase in the life expectancy of men, the need for early diagnosis and treatment of prostate diseases (pancreas) is only increasing. It should be remembered that early diagnosis of pancreatic pathology even before the clinical picture of the disease leads to an improvement in the effectiveness of their treatment. The clinical manifestation of pancreatic pathology always significantly worsens the quality of life of such patients, depresses the psychological status, sexual and reproductive functions, affects the family and professional aspects of men's life [8]. The presence of clinical symptoms of prostate cancer (prostate cancer) more often already indicates a locally advanced or generalized stage of pathology [2]. The clinical symptoms of pancreatic pathology are rather nonspecific, often even of the same type – symptoms of the lower urinary tract, pelvic pain syndrome, erectile dysfunction – which implies a comprehensive diagnosis of such patients and the final diagnosis, but differential diagnosis of prostate pathologies is often difficult by a combination of diagnoses [11, 21]. Diagnosis should be comprehensive, with all available research methods, and if suspected of prostate cancer and invasive methods, too. The wide prevalence, difficult diagnosis, and socio-economic significance of prostate cancer require an increase in the effectiveness of the diagnosis of pancreatic pathologies [21, 22].

Prostate cancer is recognized as one of the most common malignant tumors in middle-aged, elderly and senile men [8, 17]. Prostate cancer is the most common oncological pathology of men in the USA and Europe. More than a million detected

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prostate cancer were recorded in 2012 worldwide, this is 8% of all newly detected cancers in the world and 15% of newly detected cancers in men [20]. The high incidence of prostate cancer is found in North America and Europe, lower in Asia and Africa, this is due to the use of screening programs in developed countries and different levels of medicine in these countries [12, 23].

Prostate cancer is one of the most frequently detected oncological diseases in men in Russia. In the structure of morbidity of men in the Russian Federation in 2012, prostate cancer was on the 3rd place (11%), and among the general morbidity – on the 6th place (5.5%) [3]. Over the 10 years of the new millennium, the annual increase in the incidence of prostate cancer in Russia has reached 9%, and the overall increase was 137%, the rate of growth of prostate cancer is in 2nd place, second only to melanoma [9].

In the structure of oncological morbidity among the male population in Uzbekistan, prostate cancer is in 3rd place, second only to stomach and lung cancer [1].

The high prevalence of prostate cancer dictates the need to further improve early diagnosis and improve the effectiveness of diagnostic measures, because the prognosis of this pathology depends on the stage of prevalence [14].

The relevance of early diagnosis of pancreatic pathologies is undeniable in modern medicine. The widespread use of clinical, laboratory and radiation diagnostic methods has practically not solved the problem of early accurate diagnosis of prostate diseases. Practical healthcare in the diagnosis of prostate pathology often relies on the least invasive methods – finger rectal examination (FRE), the level of prostate-specific antigen (PSA) in the blood serum and transrectal ultrasound (TRUS). An increase in PSA and the prostate compaction zone are accepted as the fundamental criteria for prostate diseases [5].

All of the above prompted us to conduct a study, the purpose of which was to assess the sensitivity, specificity and accuracy of the methods used for diagnosing prostate cancer.

Material and methods

The material of the study was a group of men in the number of 156 men examined in the period from 2020 to 2021, who were examined in the urological department of the RSSPCOR of the Ministry of Health.

The main group consisted of 120 people (76.9%) and 36 people (23.1%) – the control group. The bulk of the examined patients of the main group were men on average – 40 (33.33%) and the elderly – 54 people (45.00%).

We completely excluded all infectious diseases of the urethra and prostate in all patients with a directional diagnosis of prostate cancer. In the main and control groups, we performed AT, the level of PSA in the blood serum was determined, a pancreatic ultrasound (with EDC and compression elastographic enhancement) and an MRI of the pelvic organs were performed, a targeted biopsy with histological verification of the process was taken as the basis for the diagnosis.

The bulk – 54.17% were patients with prostate cancer, and the combination of prostate cancer+BPH (benign prostatic hyperplasia) – 24.17%, due to the

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predominant age of the examined individuals, it was on these patients that the possibilities of research methods in the diagnosis of prostate cancer were studied.

The degree of histological differentiation of tumors and the stage of their invasion were evaluated according to the WHO classification and the D.F. Gleason system [13].

Patients with an established (confirmed) diagnosis of prostate cancer were divided into groups, according to the clinical classification according to TNM. The first group (T1) is a clinically determined, visualized tumor, the second group (T2) – the tumor is limited to the prostate gland, the third group (TK) – the tumor spreads beyond the prostate capsule; the fourth group (T4) – the spread of the tumor to other pelvic organs (Table 1): Table 1. Distribution of patients with prostate cancer by stages

Groups of patients	Number of patients	
	Abs	%
I group (T1)	16	13,33
II group (T2)	49	40,83
III group (T3)	32	26,67
IV group (T4)	23	19,17
Total:	120	100

Research results

All our patients complained of urination disorders. Due to the combination of several symptoms of urination disorders (SUD) in the overwhelming number of patients, the sum of clinical manifestations exceeds the total number of examined in this group, the leading SUD were stranguria – 95 (79.17%) patients, nocturia – 77 (64.17%) and difficulty urinating – 68 (56.67%) patients.

We found that in the main group of patients, nocturia and sluggishness of the urine stream had a statistically significant ($p<0.05$) dependence on age. While daytime pollakiuria, stranguria and difficulty urinating had no age dependence. Irritative symptoms prevailed in the age group up to 55 years, and obstructive symptoms prevailed over 61 years, that is, in the elderly and senile age.

Finger rectal examination was mandatory for all patients, the results of which were also taken into account when deciding whether to perform a prostate biopsy.

In 68 out of 120 (56.67%) patients, palpatory changes in the pancreatic parenchyma were detected, allowing to suspect prostate cancer (asymmetry of the lobes, an increase in the density of the palpable tissue area). At the same time, in the group of patients with suspected prostate cancer, these changes were observed in 5 out of 26 (19.23%) patients, in the group of patients with BPH+prostate cancer – in 16 out of 29 (55.17%), and in the group of patients with the direction of prostate cancer − in 47 out of 65 (72.31%) patients.

Palpatory enlargement of the prostate was found in 58 (48.33%) patients, smoothness of the interlobular furrow – in 49 (40.83%), the presence of nodular formations – in 27 (22.50%), asymmetry of the prostate lobes – in 37 (30.83%). The

palpatory density of the prostate was also determined, which was divided into four gradations: elastic – it was in 29 patients (24.17%), tightly elastic - in 38 (31.67%), dense – in 34 (28.33%) and "cartilaginous" – in 19 (15.83%).

Consequently, the pathological changes detected during FRE were detected significantly more often with a directional diagnosis of prostate cancer ($\chi 2=20.7$, $p<0.001$) and BPH+prostate cancer ($\chi 2=18.3$, $p<0.001$). It should be noted that there were no palpatory changes in 52 (43.33%) patients with morphologically confirmed prostate cancer.

In the control group, finger examination revealed changes in 2 (5.56%) patients, but no other study recorded changes in the pancreas, which confirms the influence of the human factor on the results of this method of investigation.

For FRE, the specificity was 89% with a sensitivity of 51% and an accuracy of 68%, which necessarily implies additional research methods.

In the main and control groups of patients, the serum PSA level was studied in all 156 patients. The level of total blood PSA of 4 ng/ml or more was noted in 109 (90.83%) patients of the main group. However, taking into account the age-dependent discriminatory levels, an increase in PSA was found in 104 patients (86.67%). In 16 men (13.33%), prostate cancer was detected against the background of normal PSA levels, taking into account age-specific discriminatory levels, and of these in 11 (9.17%) patients, PSA did not exceed 4 ng/ml.

At the same time, almost every fifth patient of the main group was in the so-called "gray zone", and patients with PSA of more than 30 ng/ml prevailed, which clearly confirms the increase in PSA levels in prostate cancer, but leaves the question of sensitivity debatable, taking into account the normal PSA level in 9.17% of patients.

The table shows that the level of total PSA in blood plasma and relative PSA density in patients with prostate cancer was significantly higher than in patients of the control group ($p=0.007$ and $p=0.008$, respectively).

PSA levels of more than 13.6 ng/ml were highly specific for prostate cancer, even with normal indicators of other studies, but PSA levels of less than 4 ng/ml did not exclude the presence of prostate cancer.

We have determined the sensitivity, specificity and accuracy of the PSA study for the diagnosis of prostate cancer. Thus, with PSA >4 ng/ml, sensitivity is 92%, specificity is 35% and accuracy is 59%, and with PSA >10 ng/ml -69%, 96% and 76%, respectively.

In the gray scale mode of stage II-IV prostate cancer in the vast majority of patients (94 out of 104 (90.38%)) it was displayed by a hypoechoic formation. However, the hypoechogenicity was not absolutely specific for prostate cancer, so the remaining 9.62% (10 people) of the formations in the peripheral region of the prostate were recognized by histological verification as benign, and prostate cancer was diagnosed only after surgery during histological examination.

Stage T1 of BPH (group I) was established in 16 patients who had a directional diagnosis of BPH and suspected of BPH, surgical intervention was performed for BPH (10 – transurethral resection and 6 – transubstantial adenomectomy). It should

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be understood that in each patient in this group, signs of malignant growth were histologically verified in one or two fragments of resected pancreas.

At stage T2 of prostate cancer (group II), a hypoechoic focus of the pancreatic parenchyma was found in 41 patients (83.67%) or the absence of any echographic abnormalities (8 patients - 16.33%).

At the stage of TK (group III), a diverse echographic picture was established due to local and diffuse changes.

In group III patients with stage T3 of prostate cancer, the most difficult task was to determine the germination of the pancreatic capsule. The definition of the echographic capsule of the prostate as a hyperechoic line without breaks was not obtained in milestone patients. As a result, it was possible to confirm T3 prostate cancer on the basis of extracapsular tumor spread only with asymmetric deformation of the prostate borders with an increased volume, which was recorded only in 12 (37.50%) patients with prostate cancer of the TK stage.

At stage T4 (group IV), an increase in prostate volume was noted, often with a decrease in echogenicity. With severe prostate cancer (4 patients – 17.39%), differentiation of the prostate parenchyma among the surrounding tissues was a difficult and practically impossible task, due to the lack of clear boundaries of the pancreas.

An increase in the MP wall in the cervical region was found in all 23 patients of group IV with prostate cancer in the T4 stage (100%). We found a similar thickening in 28.57% (14 patients) with prostate cancer in the T2 stage, as well as in 40.83% (49 patients) of all studied patients. Based on this, this feature is not applicable in the aspect of the diagnosis of cancer involvement of MP.

Based on the results of a survey of 156 people, we determined the sensitivity, specificity and accuracy of the TRUS, which amounted to 89%, 85% and 77%, respectively.

With TRUS, coupled with ultrasound angiography, we found markers of neovascularization in prostate cancer:

1. asymmetry of local vascularization with an increase in degree (14.17%);

2. disorganization of angiogenesis of the region (tortuosity, discontinuity, heterogeneity and randomness of vessels) (47.50%);

disproportion of the vascular tree of the region (38.33%).

Sensitivity of the TRUS coupled with ultrasound angiography was determined by us in 90%, specificity – 87% and accuracy – 89%.

The combination of ultrasound and ultrasound angiography makes it possible to more fully assess the stage of the tumor and predict, with a certain degree of probability, the reaction of cancer to conservative treatment, which is very important for practical oncology as a method of dynamic control of prostate cancer therapy.

Taking into account such ambiguous indicators, we analyzed the informativeness of the complex application of the PSA level >4 ng/ml, with and TRUS (Table 2).

Table 2 The informativeness of various methods of diagnosis of prostate cancer (%)

	Diagnostic methods

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Parameters	FRE	PSA>4 нг/мл	TRUS	PSA>4ng/ml +FRE+TRUS
Sensitivity	51	92	89	94,2
Specificity	89	35	85	83,9
Accuracy	68	59	77	78,4

Thus, a comprehensive diagnostic approach with high sensitivity (94.2%) significantly increases specificity (83.9%) and accuracy (78.4%). This makes it possible to more accurately refer patients to a pancreatic biopsy and reduce the frequency of its negative responses.

All patients in our study underwent pancreatic MRI. The prostate was detected on all scans, but worse in the coronary projection. The contours of the pancreas were well visualized in T2 mode, especially on transverse images, due to a significant difference in the intensity of the signal from the prostate and paraprostatic veins. The parenchyma of the gland was characterized by heterogeneity, especially in the T2 mode. The structure of the pancreas on MRI in T1 mode was indeterminate, but the paraprostatic fiber clearly outlined the gland and soft tissues of the pelvis with an intense signal. Particular attention was paid to the detection on axial MRI images of neurovascular nodes on the sides in the triangular fatty spaces between the pancreas and the rectum. Determination of the structure and allocation of prostate zones was carried out on T2 images. The normal peripheral zone on them had a high intensity – it was displayed as light, and the dark central and intermediate zones, difficult to distinguish between each other, were hypointensive, in the latter, BPH often occurred.

In 16 patients (13.33%), the spread of prostate cancer into paraprostatic tissue was detected, which was manifested by hypointensive foci with fuzzy boundaries. The intact wall of the MP in the T2 mode was visualized clearly and was a dark hypointensive strip, but was more intense than its contents of the bubble in the T1 mode. In case of damage to the wall of the MP RP, a decrease in clarity, the appearance of irregularities and discontinuity of the contours of the wall with hyperintensive foci were noted.

The use of paramagnetic contrast agents did not enhance the diagnostic capabilities of MRI for prostate cancer. The T2 images even surpassed the images of the T1 mode with contrast, more reliably and accurately assessing the condition of the gland. MRI makes it possible to diagnose the involvement of neighboring organs in the process and identify regional metastases, which specifies the stage of the process and determines the tactics of patient treatment and dynamic monitoring of its effectiveness. T1 images in the axial and frontal planes are the most informative.

For MRI in the diagnosis of prostate cancer, we calculated sensitivity of 89.4%, specificity – 78.2% and accuracy – 74.5%

In our study, all patients underwent puncture biopsy on an outpatient basis under local anesthesia, punctures were performed and material was taken from different areas of the pancreas (multifocal biopsy). 8 biopsies were taken and

examined: peripheral, central and transitional zones of each lobe and two seminal vesicles. This technique of biopsy makes it possible to identify the early stages of prostate cancer. The conclusion of the histological examination of 8 prostate biopsies obtained under the control of TRUS was the final diagnosis in our study.

Our patients were diagnosed with prostate cancer (adenocarcinomas and solid cancers) and pancreatic sarcoma. According to the cellular composition, dark-cell and light-cell adenocarcinomas were found.

Microscopically, prostate cancer was characterized by the appearance of glandular structures with pathology of the normal structure of the pancreas, namely, the absence of a linear pattern and the close location of groups of acinuses.

The histologist was also tasked with determining the presence of prostatic intraepithelial neoplasia (PIN) in the preparations of our patients. PIN is manifested by a certain degree of proliferation of secretory epithelium in the lumen of the glands, the maximum of which is indistinguishable from carcinoma [10]

A high degree of PIN is often located in the immediate vicinity of invasive adenocarcinoma, especially in the peripheral zone of the prostate [18].

The close relationship of these pathologies is not proof of the theory that a high degree of PIN is a precursor to cancer [15]. There is an opinion that they are caused by identical etiological factors, but the PIN finding is insufficient and unnecessary for an accurate prediction of the occurrence of adenocarcinoma [19, 23]. The study of prostate cancer in patients aged 30-40 years practically did not reveal PIN, since the peak of PIN detection occurs at the age of 60 years, and with early detection of prostate cancer, PIN 3 is often not detected [18].

The average occurrence of PIN 3 among our patients was 35.83%, with a minimum in the T1 group – 31.25% and a maximum at T4 – 39.13%. Moreover, 88.37% were patients aged 58-63 years. These data confirm the opinion of Taylor T. about the peak occurrence of PIN 3 in 60 years and the absence of evidence of the antecedence of PIN RPJ [17].

The sensitivity of transrectal multifocal biopsy of the pancreas under the control of TRUS is 86.1%, specificity is 98.3%, and accuracy is 99.4%.

Conclusions

1. FRE is only one of the purely subjective methods of pancreatic examination, entirely dependent on the experience of the doctor conducting the research and can only be a starting point for further examination of the patient.

2. The determination of blood PSA is a fairly effective marker in the diagnosis of prostate cancer in the screening examination in the age group up to 60 years, allowing suspecting prostate cancer at levels of total blood PSA within the "gray zone", i.e. at the level of PSA from 4 to 10 ng / ml. A PSA level of more than 13.6 ng/ml is highly specific for prostate cancer, but a PSA level of less than 4 ng/ml did not exclude the presence of prostate cancer, which requires further stages of a comprehensive study of patients with suspected prostate cancer.

3.TRUZI provides reliable and valuable diagnostic information about the prostate parenchyma, which is used not only for prostate cancer, but also for other pancreatic pathologies, given the very high image quality and detailed visualization of the structures of the gland, surrounding organs and tissues, and allows for a targeted biopsy from a specific area of the prostate.

4. The proposed echographic markers of prostate cancer contribute to the early diagnosis of the disease and significantly accelerate the appointment of conservative treatment of this pathology, can reduce the number of invasive diagnostic interventions, which is relevant when elderly and senile patients predominate in this pathology.

5.A comprehensive diagnostic approach (PSA>4ng/ml+ AT+ TRUS) with high sensitivity (94.2%) significantly increases specificity (83.9%) and accuracy (78.4%). This makes it possible to more accurately refer patients to a pancreatic biopsy and reduce the frequency of its negative responses.

6.The final diagnosis of prostate cancer rightfully remains for transrectal multifocal biopsy of the pancreas under the control of TRUS with a sensitivity of 86.1%, specificity – 98.3%, and accuracy – 99.4%.

References

1. Tillyashaikhov M.N., Ibragimov Sh.N., Dzhanklich S.M. The state of oncological care for the population of the Republic of Uzbekistan in 2019. - Tashkent, 2020. - 124 p.
2. Aleksandrov V.P., Karelin M.I. Prostate cancer. St. Petersburg: SPbMAPO Publishing House. - 2004. 148 p.
3. Apolikhin O.I., Sivkov A.V., Moskaleva N.G. et al. Analysis of uronephrological morbidity and mortality in the Russian Federation over a ten-year period (2002-2012) according to official statistics // Experimental and Clinical Urology. - 2014. - No. 2. From 4-12.
4. Kaprin A.D., Kostin A.A., Kulchenko N.G. et al. Screening for prostate cancer based on multivariate analysis // Bulletin of the Medical Institute "REAVIZ": rehabilitation, doctor and health. - 2014. - No. 4. - P.38-42.
5. Katibov M.I., Voitko D.A. Selective screening as a new approach to improve the efficiency of diagnosis and treatment of prostate cancer. // Collection of abstracts of the 10th anniversary congress of the professional association of andrologists of Russia. - 2015. - S. 55
6. Pushkar D.Yu., Kolontarev K.B., Alekseev B.Ya. et al. Urology. Russian clinical guidelines. Moscow. - 2016. 492p.;
7. Rodoman V.E., Avdoshin V.P., Kolesnikov G.P. Diseases of the prostate. M.: Medical information agency. - 2009. - 667s.
8. Chissov V.I., Starinsky V.V., Petrov G.V. Malignant neoplasms in Russia in 2010 (morbidity and mortality) M.: FGBU "MNIOI im. P.A. Herzen" of the Ministry of Health and Social Development of Russia. 2012. - s100Berry SL, Boczkowski A, Ma R, Mechalakos J, Hunt M. Interobserver variability in radiation therapy plan output: Results of a single-institution study. // Pract Radiat Oncol. 2016 Nov-Dec;6(6):442-449. doi: 10.1016/j.prro.2016.04.005. Epub 2016 May 8.
9. Collins M.M., Meigs J.B., Barry M.J. et al. Prevalence and correlates of prostatitis in the health professional's follow-up study cohort // J. Urol. - 2020. - 167(№ 3). - P. 1363-1366.;
10. Hamdi Y, Abdeljaoued-Tej I, Zatchi AA, Abdelhak S, Boubaker S, Brown JS, Benkahla A. Cancer in Africa: The Untold Story. // Front Oncol. 2021 Apr 15;11:650117.
11. Mariotti GC, Costa DN, Pedrosa I, et al. Magnetic resonance/transrectal ultrasound fusion biopsy of the prostate compared to systematic 12-core biopsy for the diagnosis and characterization of prostate cancer: multi-institutional retrospective analysis of 389 patients. // Urol Oncol. – 2016. - №34(9). – p.416.e9-e14
12. Mukherjee S, Sudandiradoss C. Transcriptomic analysis of castration, chemo-resistant and metastatic prostate cancer elucidates complex genetic crosstalk leading to disease progression. // Funct Integr Genomics. 2021 Jul;21(3-4):451-472.
13. Nelms B, Stambaugh C, Hunt D, Tonner B, Zhang G. Methods, software and datasets to verify DVH calculations against analytical values: Twenty years late(r). // Med Phys. 2015 Aug;42(8):4435-48.

14. Phua T.J. The Etiology and Pathophysiology Genesis of Benign Prostatic Hyperplasia and Prostate Cancer: A New Perspective. // Medicines (Basel). 2021 Jun 11;8(6):30.
15. Siegel R., Naishadham D., Jemal A. Cancer statistics, 2012. // CA Cancer Journal for Clinicians. - 2012. - vol. 62. - no. 1. - pp. 10-29
16. Taylor T, Richmond N. A UK wide study of current prostate planning practice. // Br J Radiol. 2020 Jul;93(1111):
17. Villaggi E, Hernandez V, Fusella M, Moretti E. Plan quality improvement by DVH sharing and planner's experience: Results of a SBRT multicentric planning study on prostate. // Phys Med. 2019 Jun;62:73-82.
18. Waddell AR, Huang H, Liao D. CBP/p300: Critical Co-Activators for Nuclear Steroid Hormone Receptors and Emerging Therapeutic Targets in Prostate and Breast Cancers. // Cancers (Basel). 2021 Jun 8;13(12):2872.
19. Wang G, Zhao D, Spring DJ, DePinho RA. Genetics and biology of prostate cancer. Genes Dev. 2018 Sep 1;32(17-18):1105-1140.
20. Widjaja L, Werner RA, Ross TL, Bengel FM, Derlin T. PSMA Expression Predicts Early Biochemical Response in Patients with Metastatic Castration-Resistant Prostate Cancer under 177Lu-PSMA-617 Radioligand Therapy. // Cancers (Basel). 2021 Jun 11;13(12):2938.
21. Wright K, Ferrari-Anderson J, Barry T, Bernard A. Improving plan quality for prostate volumetric-modulated arc therapy. // Med Dosim. 2017 Winter;42(4):348-356. doi: 10.1016/j.meddos.2017.07.001. Epub 2017 Aug 4.
22. Zhu Y, Mo M, Wei Y, Wu J, Pan J, Freedland SJ, Zheng Y, Ye D. Epidemiology and genomics of prostate cancer in Asian men. // Nat Rev Urol. 2021 May; №18(5) – p.282-301. doi: 10.1038/s41585-021-00442-8. Epub 2021 Mar 10.