

The Role of Hormone Therapy in Prostate Cancer

Rakmanov Xamza Abdukadirovich

Assistant, Department of Clinical Pharmacology, Samarkand State Medical University

Abstract: Brachytherapy allows most patients to maintain potency and reduces the risk of urinary incontinence. But, again, there are a number of nuances that prevent brachytherapy from becoming the "gold standard", among which:

the inability to correctly stage the tumor process and determine the radicality of the treatment (there is no sample taken from the prostate and lymph nodes);

the method is suitable only for patients with a minimal degree of tumor process (not even for all cases of local prostate cancer);

prostate size restrictions - the procedure is not suitable for patients with severe urinary disorders (difficulty urinating, slow urine flow, frequent urination, strong urges, repeated nighttime trips to the toilet, onset of urinary incontinence, etc.);

The postoperative period is often complicated by problems such as acute urinary retention, which requires additional therapeutic measures.

Key points: HIFU (High Intensity Focused Ultrasound) - high intensity focused ultrasound.

One of the relatively new methods of local treatment of prostate cancer. The essence of the method is that through a sensor located in the patient's rectum, under ultrasound control, a targeted thermal effect is applied to the prostate tissue, which leads to the death of tumor cells.

Although it is "young", this approach is very common in the world. Indeed, the least invasive (traumatic) of all methods of treating prostate cancer is very effective (in experienced hands).

It should be noted that HIFU is a very capricious procedure that requires very careful selection of "suitable" patients. This choice largely depends on the effectiveness of the procedure (suitable only for patients with very early forms of cancer) and the probability of complications, unfortunately not so low (acute urinary retention, stenosis of the prostate urethra, urinary incontinence, etc.). The technique is in any case promising, but it is too early to talk about its role in the treatment of prostate cancer.

Hormone therapy for prostate cancer

Prostate cancer is a disease whose development depends on the level of male sex hormones (androgens) in the blood. The lower their level, the slower the tumor grows. Therefore, another method of treating prostate cancer is hormone therapy, which is a maximum androgen "blockade". For local cancer, this approach is used only as an adjunct to the main treatment.

The simplest, cheapest and relatively safe way to reduce the level of sex hormones is bilateral removal of testicular tissue (surgical castration). Today, this is the "gold standard" of antiandrogen therapy. It is clear that this approach is very unpleasant for many patients, because in their opinion, they are "deprived of masculinity." There is another method of treatment - medical "castration", when drugs that block the production of androgens are prescribed. Modern drugs of this group are close to testicular tissue removal in terms of effectiveness and safety.

Prostate Cancer Treatment Plan

Locally advanced prostate cancer spreads beyond the organ, but does not affect nearby structures and does not metastasize.

Treatment of this form of prostate cancer is a very complex and controversial issue. The decision on the method of treatment should be made strictly individually and on the basis of a comprehensive examination. In any case, treatment of patients with locally advanced prostate cancer should be comprehensive. For operable patients, this can be followed by radical (adjuvant) prostatectomy with radiation therapy and/or a combination of hormone therapy. Or independent use of radiation therapy, and then hormone therapy, etc. The use of modern methods of treating this category of patients allows us to ensure a 5-year survival rate of 70-80%.

Metastatic (common) prostate cancer, despite the 21st century, has come to our country for a long time, unfortunately, it is rare. Most often, an advanced malignant tumor of the prostate is the result of the imperfection of the health care system, illiteracy of a certain doctor and negligence of the patient. Many patients tell us that they went to the doctor "5 years ago" with symptoms of "prostatitis" or "adenoma" and since then they have been receiving constant (and less) treatment. And when you ask such a patient: "Have you donated blood for PSA?" You get the traditional answer: "What is it?" Until the situation changes dramatically, urological oncologists will have to diagnose every fourth patient.

The main feature of common prostate cancer is the presence of metastases in the lymph nodes, bones, lungs, liver and other organs. With this form of the disease, there is no point in removing the prostate or exposing it to radiation. A competent doctor can do only two things (not counting spiritual support):

slow down the development of the tumor process and thus prolong the patient's life (hormone therapy, if it is ineffective, cytotoxic therapy);

improve the patient's quality of life and/or combat potentially fatal complications of prostate cancer (improving urine flow, stopping bleeding, relieving pain, preventing bone fractures due to metastases, etc.).

Our work was aimed at identifying people with prostate cancer, verifying the diagnosis using two well-known diagnostic methods (PSA prostate-specific antigen, digital rectal examination, transrectal ultrasound, transrectal dopplerography of prostate vessels) and a new method - histoscopy. In the course of the work, a comparative analysis of standard research methods and diagnostic capabilities of histoscan for prostate cancer and hyperplasia was carried out. In addition, the diagnostic value of the method related to early detection of cancer, the accuracy of staging the process and the impact of the results obtained on the planning of polyfocal prostate biopsy and the choice of subsequent treatment tactics were determined.

First, a retrospective group of patients (hereinafter referred to as the first group) was identified and examined: 67 patients with suspected prostate cancer underwent prostate biopsy between 2009 and 2011. It performed a standard diagnostic complex for a patient with suspected prostate cancer, consisting of clinical and biochemical blood tests, detection of prostate-specific antigen (total and, according to the instructions, free (total PSA > 4 ng/ml), PSA density), general urine analysis, 3-well test, uroflowmetry, transabdominal and transrectal ultrasound of the prostate, as well as Doppler ultrasound of the prostate vessels, after which a transrectal polyfocal biopsy was performed.

Then, to directly address the aims and objectives of our study, we examined 701 patients using the Histoscan device. All these patients underwent the standard diagnostic complex mentioned above. The distribution of prostate-specific antigen levels was from 1.09 to 209 ng/ml.

Patients with elevated PSA levels who underwent histoscopy were divided into 3 groups based on the degree of increase. Thus, 67 patients (to compare prostate biopsy results with and without histoscopy) and two control groups were identified.

In the first four groups (patients with suspected prostate cancer), all patients underwent a prostate biopsy.

With the introduction of HistoScan, each patient arriving at our clinic with an elevated PSA level (or with a normal PSA level, but prostate cancer was suspected by other examination methods) was assigned to one of the above groups. Then, the patients were examined according to the scheme developed for this study. This was a classic examination of a patient suspected of prostate cancer. The first step was a digital rectal examination (DRE). Seven (1.5%) of the 456 patients in the second group had areas suspicious of prostate cancer. In the third group of 112 patients, 17 (15.3%) DREs were suspicious of cancer. In the fourth group, during DRE, 63 out of 70 patients had suspicious areas, which was 87.5% of the patients in this group. In the fifth group – a conditional control group – none of the 20 patients had any suspicious areas detected during digital rectal examination. In the sixth group, none of the subjects had suspicious areas during DRE.

In the first group of 67 patients, 15 (22.3%) had areas suspicious for prostate cancer on digital rectal examination (Table 2).

Identification of suspicious areas during DRE in patients from research groups.

After that, a classic gray ultrasound - transabdominal and transrectal examination was performed, after which a Doppler examination was performed. According to the examination data, the presence or absence of foci suspicious for prostate cancer was recorded (Figure 6). It should be mentioned here that we did not take into account changes according to TRUS and Doppler data, characteristic of prostatitis and prostate adenoma.

In none of the 456 patients in the second group, we found changes characteristic of prostate cancer according to TRUS and Doppler examination of blood flow of prostate vessels. In the third group with PSA thresholds of 10-20 ng/ml, no ultrasound signs of prostate cancer were found in any of the patients, as in the second group. In the fourth group, 30 out of 70 patients, or 43.8%, have ultrasound signs characteristic of prostate cancer. In the fifth group, TRUS and Doppler ultrasound of the prostate did not reveal changes specific to prostate adenocarcinoma in any of the patients. No changes were found in the young people of the sixth (control) group.

In the first group of 67 patients, 11 had classic hypoechoic areas suspicious for prostate cancer, or 16.4% of all patients in the group.

The second step of the study consisted of performing a histoscopy with prostate mapping for biopsy. Histoscopy begins with a transrectal ultrasound.

Transrectal ultrasound is performed in two projections: the prostate is imaged in transverse projection, then in sagittal projection. Then the prostate is scanned in the sagittal plane. This is possible due to the fact that the sensor is mounted on a special magnetic coil that rotates 180° when it is in the rectum.

After that, the ultrasound data of the prostate are processed by the HistoScan device. During processing, the histoscan creates three projections of the prostate. The first two - sagittal and transverse - are obtained by ultrasound.

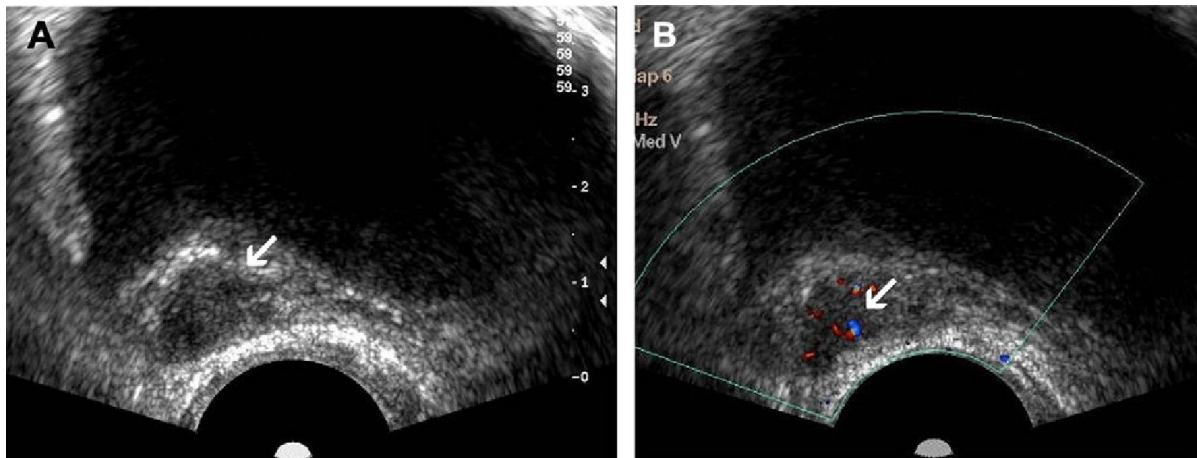
Prostate with construction of a 3D model in 3 projections.

Prostate gland in 3 projections and 3D model with histoscopic tissue (suspected of prostate cancer) shown in green.

In the 3D model, the histoscan tissue (suspicious for prostate cancer) is shown in green.

Then, the HistoScan device (hereinafter referred to as histoscan), based on these data, independently constructs the third virtual plane of the prostate - frontal (cranial). Based on the information obtained from the three projections, the histoscan creates a 3D model of the prostate, which can be oriented in space according to the needs of the researcher.

After creating all the prostate projections and creating a 3D model, the researcher further defines the boundaries of the prostate, which he first defines independently. The ultrasound data of the prostate are then processed by the Histoscan device. Thus, in the 3D model, we obtained areas suspicious of prostate cancer. Then, a prostate map was created for biopsy, where the areas suspicious of prostate cancer were also marked.



In the third stage of the study, some patients with a high risk of cancer, i.e. some patients in groups 3 and 4, underwent MRI with an endorectal coil, and several of them additionally underwent CT scanning of the pelvic organs.

The fourth stage of the examination was a polyfocal transrectal biopsy of the prostate under ultrasound guidance for patients in groups 2, 3 and 4 (groups 1, 5 and 6 - control).

It should be noted here that, unlike patients of the first group, in this case, the prostate biopsy was performed according to the prostate maps obtained by histoscaning. To facilitate the evaluation of the results of the technique, each studied prostate is divided into 6 zones - sextants. Histoscan provides information in cubic centimeters about the volume of each of these sextants, as well as the volume of pathological tissue in a given sextant. The device then adds and displays the total volume of the gland, as well as the total volume of lesions suspicious for prostate cancer in the specific prostate studied. This information, due to computer processing, is more accurate than the size of the gland measured during ultrasound.

Note that the number of sextants for each patient is constant and equal to 6 (Figure 2). But the number of sites taken during biopsy varied and depended on the size and number of suspicious sites according to histoscopy. Biopsies from these areas were considered suspicious. We assessed the presence or absence of a suspicious lesion based on the histoscopic data of a certain sextant and then on the morphological picture of this area - this is the first way to compare the data of histological examination and the morphological conclusion. The morphological results of the study were the gold standard for detecting prostate cancer. Then, the data from all studies were compared with each other.

Sextants in the prostate.

Prostate sextants - sagittal projection on the left, cranial on the right (suspected prostate cancer tissue is shown in pink)

Sagittal projection of the prostate on the left, cranial projection on the right. Pink in both projections indicates tissue suspicious for prostate cancer. Arrows in the cranial projection of the prostate indicate sextants.

Also, in order to optimize and simplify the calculation of the results of patient examination using histoscan, a second method for assessing the sensitivity and specificity of histoscan was developed. First, we counted the number of tissue cores obtained from suspicious areas during polyfocal prostate biopsy for each patient and summed their number. These were standard sutures of tissue

taken from suspicious areas and additional sutures taken from suspicious areas. For example, the total number of suspicious columns of prostate tissue in the second group of patients was 2,684.

Second, in the same way, we calculated for each of these patients the number of columns of tissue obtained during polyfocal biopsies of the prostate from areas not modified according to histoscan. The number of these columns of prostate tissue was 3,700. In other words, the number of columns of non-suspect prostate tissue was 3,700. This number constitutes the standard column of prostate tissue.

Sampling scheme for tissue columns for prostate biopsy.

Tissue column sampling scheme for prostate biopsy

Prostate map, arrows indicate sites of additional tissue sampling during prostate biopsy. Thus, a total of 16 columns of prostate tissue were obtained from this patient: 12 standard and 4 from suspicious sites.

Histoscan map.

Histoscan Map - locations of collections in additional columns are indicated by arrows

Grid locations for additional messages are indicated by arrows.

Then, we evaluated the morphological image of all prostate tissue columns and compared it with the histoscan results.

After receiving these data, we calculated the sensitivity and specificity of the method for detecting prostate cancer using the Histoscan device.

In addition to the above, we developed a third method for assessing the morphological picture of suspicious areas according to histoscopic data, which consists in performing an additional postoperative biopsy after radical prostatectomy, in which both suspicious areas and unchanged tissues according to histoscopic data are taken. For this purpose, the removed gland is specially marked in 5×5 mm quadrants. This feature made it possible to correctly spatially project suspicious areas from histoscopy data into the prostate. After numbering the tissue columns, we sent them for morphological examination, which was performed blindly, i.e. the morphologists did not know which areas of the prostate they were examining (Figure 3).

Comparison of prostate mapping for blinded postoperative biopsy.

Photo of the removed prostate on the left, histoscopic plane on the right

On the left is a photograph of the removed prostate (specially marked 5×5 mm), on the right is a map taken from a histoscan (also marked 5×5 mm).

The data of the morphological study were then compared with the data of histoscopy. This comparison was carried out in collaboration with expert morphologists after radical prostatectomy. It should be noted here that there are several methods of postoperative assessment of the prostate. We used the following method: first, the entire prostate was cut by a morphologist as an "open book": sections of the organ were made from the base to the apex with a slice 2-3 mm thick and were incomplete. end, that is, in comparison with an open book, the area became "the binding of this book". The results of the morphological study fully confirm the data of the histoscan: according to the data of the histoscan, the node is macroscopically located in the right lobe, and during the morphological study, the node is adjacent to the prostate capsule in the right lobe (Fig. 5); .

Macroscopic specimen and map of the prostate.

A macroscopic sample of the prostate - part of the tumor tissue is surrounded in red

A. Macroscopic preparation of the prostate in open book view, with some tumor tissues circled in red.

Schematic map of the prostate - blue arrow indicates dotted line

B. Prostate map with dotted line indicated by blue arrow.

Thus, using histoscan data, 638 prostate biopsies were performed, their morphological results were compared with data from 67 prostate biopsies performed without histoscopic data, as well as with data from 53 morphological studies after prostatectomy.

List of literature used:

1. EAU, Richtlinien, 2011.
2. Prostataerkrankungen. Herausgegeben von Yu G. Alyaev. GEOTAR – Medien, 2009.
3. Alyaev Yu.G., Amosov MA, Vinarov AZ, Lokshin KL, Spivak LG Transrektale Dopplerographie bei Patienten mit Prostataerkrankungen / FGUIPP „Kostroma“, 2004, 88 S.
4. Долиев, М. Н., Тулакова, Г. Э., Кадырова, А. М., Юсупов, З. А., & Жалалова, Д. З. (2016). Эффективность комбинированного лечения пациентов с центральной серозной хориоретинопатией. Вестник Башкирского государственного медицинского университета, (2), 64-66.
5. Zukhridinovna, Z. D. (2022). Modern aspects of neuroprotective treatment in hypertensive retinopathy.
6. Jalalova, D., Raxmonov, X., & Shernazarov, F. (2022). THE ROLE OF C-REACTIVE PROTEIN IN THE PATHOGENESIS OF VISUAL VASCULAR DISEASES IN PATIENTS WITH ARTERIAL HYPERTENSION. Science and Innovation, 1(8), 114-121.
7. Jalalova, D., Raxmonov, X., & Shernazarov, F. (2022). SIGNIFICANCE OF ENDOTHELIAL DYSFUNCTION IN THE DEVELOPMENT OF RETINOPATHY IN PATIENTS WITH AN AND WAYS OF ITS CORRECTION. Science and Innovation, 1(8), 101-113.
8. Jalalova, D., Axmedov, A., Kuryazov, A., & Shernazarov, F. (2022). COMBINED DENTAL AND EYE PATHOLOGY. Science and innovation, 1(8), 91-100.
9. Саттарова, Х. С., Жалалова, Д. З., & Бектурдиев, Ш. С. (2011). Причины слепоты и слабовидения при сахарном диабете. Академический журнал Западной Сибири, (6), 27-28.
10. Arunachalam, S. (2008). The science race continues in Asia. Current Science (00113891), 94(7).
11. Zukhriddinovna, Z. D. (2022). Development of Classification Criteria for Neuroretinal Ischemia in Arterial Hypertension. Central Asian Journal of Medical and Natural Science, 3(3), 59-65.
12. Жалалова, Д. З., & Исмоилов, Ж. Ж. (2024). ТЕОРЕТИЧЕСКОЕ ОБОСНОВАНИЕ ИССЛЕДОВАНИЯ ЭНДОТЕЛИНА-1 И Д-ДИМЕРОВ В КРОВИ И СЛЕЗНОЙ ЖИДКОСТИ ПАЦИЕНТОВ С ГИПЕРТОНИЧЕСКОЙ АНГИОРЕТИНОПАТИЕЙ. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 3(3), 294-299.
13. Киселева, Т. Н., Ежов, М. В., Аджемян, Н. А., Танковский, В. Э., & Ильина, Н. В. (2016). Особенности регионарного глазного кровотока при артериальной гипертензии I-II степени и субклиническом атеросклерозе. Российский офтальмологический журнал, 9(3), 26-33.
14. Жалалова, Д. З., Кадилова, А. М., & Хамракулов, С. Б. (2021). Исходы герпетических кератоуевитов на фоне лечения препаратом «офтальмоферон» в зависимости от иммунного статуса пациентов. междисциплинарный подход по заболеваниям органов головы и шеи, 103.
15. Дроздова, Е. А., & Хохлова, Д. Ю. (2015). Морфометрическая характеристика макулярной зоны у пациентов с окклюзией вен сетчатки по данным оптической когерентной томографии. Медицинский вестник Башкортостана, 10(2 (56)), 64-67.

16. Jalalova, D., Axmedov, A., Kuryazov, A., & Shernazarov, F. (2022). СОЧЕТАННАЯ СТОМАТОЛОГИЧЕСКАЯ И ГЛАЗНАЯ ПАТОЛОГИЯ. *Science and innovation*, 1(D8), 91-100.
17. Zhang, S., & Melander, S. (2014). Varicose veins: Diagnosis, management, and treatment. *The Journal for Nurse Practitioners*, 10(6), 417-424.
18. Жалалова, Д. З., & Бабаев, С. А. (2024). РЕЗУЛЬТАТЫ ОЦЕНКИ УРОВНЯ ЭНДОТЕЛИНА-1 И Д-ДИМЕРОВ В СЛЕЗНОЙ ЖИДКОСТИ У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ. *AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI*, 3(3), 300-307.
19. Zukhriddinova, Z. D. (2022). Development of Classification Criteria for Neuroretinal Ischemia in Arterial Hypertension. *Central Asian Journal of Medical and Natural Science*, 3(3), 59-65.
20. Klinische Richtlinie 58 des National Institute for Health and Clinical Excellence (NICE), Prostatakrebs: Diagnose und Behandlung, 2008.
21. Rustamovich, A. I., Negmatovich, T. K., & Fazliddinovich, S. D. (2022). БОЛАЛИКДАН БОШ МИЯ ФАЛАЖИ ФОНИДА РИНОСИНСИТИ БОР БЕМОЛЛАРДА БУРУН БЎШЛИГИ МУКОЦИЛИАР ТРАНСПОРТИ НАЗОРАТИ ТЎҒРИСИДАГИ ЗАМОНАВИЙ ҚАРАШЛАР (адабиётлар шарҳи). *JOURNAL OF BIOMEDICINE AND PRACTICE*, 7(2).
22. Абдурахмонов, И. Р., & Шамсиев, Д. Ф. (2021). Эффективность применения местной антибиотикотерапии в лечении параназального синусита у детей с церебральным параличом. In *НАУКА И ОБРАЗОВАНИЕ: СОХРАНЯЯ ПРОШЛОЕ, СОЗДАЁМ БУДУЩЕЕ* (pp. 336-338).
23. Абдурахмонов, И. Р., & Шамсиев, Д. Ф. (2021). Болаликдан бош мия фалажи билан болалардаги ўткир ва сурункали параназал синуситларни даволашда мукорегуляр дори воситасини самарадорлигини ўрганиш. *T [a_XW [i [S US S_S^[ùe YfcS^*, 58.
24. Siddikov, O., Daminova, L., Abdurakhmonov, I., Nuralieva, R., & Khaydarov, M. OPTIMIZATION OF THE USE OF ANTIBACTERIAL DRUGS DURING THE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE. *Turkish Journal of Physiotherapy and Rehabilitation*, 32, 2.
25. Тураев, Х. Н. (2021). Абдурахмонов Илхом Рустамович Влияние будесонида на качество жизни пациентов с бронхиальным обструктивным синдромом. *Вопросы науки и образования*, 7, 132.
26. Абдурахманов, И., Шамсиев, Д., & Олимжонова, Ф. (2021). Изучение эффективности мукорегулярных препаратов в лечении острого и хронического параназального синусита при детском церебральном параличе. *Журнал стоматологии и краниофациальных исследований*, 2(2), 18-21.
27. Абдурахмонов, И. Р., & Шамсиев, Д. Ф. (2023). БОШ МИЯ ФАЛАЖИ ФОНИДАГИ ПАРАНАЗАЛ СИНУСИТЛАРНИ ДАВОЛАШДА ЎЗИГА ХОС ЁНДАШИШ. *MedUnion*, 2(1), 14-26.
28. Орипов, Р. А., Абдурахмонов, И. Р., Ахмедов, Ш. К., & Тураев, Х. Н. (2021). ОСОБЕННОСТИ ПРИМЕНЕНИЕ АНТИОКСИДАНТНЫХ ПРЕПАРАТОВ В ЛЕЧЕНИИ НЕЙРОДЕРМИТА.
29. Ахмедов, Ш. К., Тураев, Х. Н., Абдурахмонов, И. Р., & Орипов, Р. А. (2021). НЕКОТОРЫЕ ОСОБЕННОСТИ ТАКТИКИ ПРОДУКТИВНОГО ЛЕЧЕНИЯ ХРОНИЧЕСКОЙ КРАПИВНИЦЫ.
30. Абдурахмонов, И. Р. (2021). Исследование мукоцилиарной транспортной функции слизистой оболочки полости носа у больных с параназальным синуситом на фоне

детского церебрального паралича. In Актуальные аспекты медицинской деятельности (pp. 256-259).

31. Абдурахмонов, И. Р., & Тураев, Х. Н. (2022). ОПЫТ ПРИМЕНЕНИЯ СИНУПРЕТА С АНТИБАКТЕРИАЛЬНЫМИ ПРЕПАРАТАМИ В КОМПЛЕКСНОЙ ТЕРАПИИ РИНОСИНУСИТОВ У БОЛЬНЫХ ДЕТСКИМ ЦЕРЕБРАЛЬНЫМ ПАРАЛИЧОМ. Достижения науки и образования, (2 (82)), 88-92.
32. Abdurakhmanov, I., & Shernazarov, F. (2023). SPECIFIC ASPECTS OF TREATMENT OF CHRONIC RHINOSINUSITIS IN CHILDREN. Science and innovation, 2(D10), 164-168.
33. Braeckman J., Autier P., Zatura F., Peltier A., Romics I., Stenzl A., Emberton M. Bewertung von HistoScanning™ zur Erkennung, Lokalisierung und Größenbestimmung von Prostatakrebs: Ergebnisse der offenen Phasenstudie PHS-02 // J Clin Oncol 29:2011 (Suppl 7; Abstr 55).