

## The Practical Importance of Immunohistochemical Examination in Prostate Cancer

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**Abstract:** Transrectal ultrasound (TRUS) has traditionally been considered the primary imaging test of the prostate and is clinically important in both benign and malignant lesions, including benign prostatic hyperplasia (BPH), prostatitis, obstructive infertility, and prostate cancer (PCa). information. Currently, the main reasons patients are referred for TRUS are ultrasound for prostate cancer detection and evaluation and prostate biopsy. The accuracy of these studies depends in part on the cost of fixed ultrasound scanners. Transrectal ultrasound (TRUS) has traditionally been considered the primary imaging test of the prostate, providing clinically important information in both benign and malignant lesions, including benign prostatic hyperplasia (BPH), prostatitis, obstructive infertility, and prostate cancer (PCa). . Currently, the main reasons patients are referred for TRUS are ultrasound for prostate cancer detection and evaluation and prostate biopsy.

**Key points:** Anterior fibromuscular tissue, Capsule, Periprostatic adipose tissue, Periprostatic lymph nodes, Neurovascular bundles, Ejaculatory ducts.

### ULTRASOUND ANATOMY

The average dimensions of the normal adult prostate are 4.0–4.5 cm, 2.5–3.0 cm, and 3.0–4.0 cm in the transverse, anteroposterior, and craniocaudal directions, respectively. This gland is surrounded by a thin pseudocapsule, almost indistinguishable from the surrounding fascial planes. Anatomically, the neurovascular bundles that pierce the prostatic capsule are very important, as they are the main site of weakness of the capsular apparatus and are likely to be involved in the tumor process. The picture of a normal gland in TRUS depends on age. While younger men show less hyperplasia of the glandular tissue, older men develop BPH and the prostate becomes a larger gland with a more rounded shape.

On average, 70% of the normal prostate consists of glandular elements and the remaining 30% is fibromuscular stroma. The glandular tissue of the prostate usually consists of internal glands, which include the transition zone and periureteral glandular tissue, and external glands occupying the peripheral and central zones. TRUS can distinguish the transition zone, which is usually located anteriorly as a hypoechoic region, from the peripheral zone, which is echogenic and uniform in echotexture compared with the rest of the gland. In contrast, the central zone is almost no different from the peripheral zone in healthy adult men. The transition zone is the primary site of hyperplastic changes and constitutes the majority of prostate tissue in older men and may be the site of development of approximately 20% of prostate cancers. It is noteworthy that 1–5% of prostate cancers are located in the central zone. The peripheral zone, which is the main site of development of chronic prostatitis, accounts for approximately 70% of prostate cancers. In contrast, transition zone cancer lesions are unlikely to be distinguished from BPH nodules by TRUS.

### Scanning technique

Today, biplane transducers as well as end and side transducers allow multiplane imaging in semicoronal, axial and sagittal projections during transrectal scanning of the prostate. Technically,

5-8 MHz transducers provide high accuracy for the peripheral part of the gland, which is very important for accurate sample selection during biopsy. Air bubble artifacts negatively affect image quality, which can be avoided by using ultrasound gel applied to a latex condom placed over the transducer. Self-enema before the procedure helps to evacuate gas and debris, another factor that can cause distortion of the TRUS image. Simultaneous digital rectal examination can be useful to identify suspicious findings during physical examination associated with TRUS abnormalities. Many specialists prefer the left lateral decubitus position because it is well tolerated. In conclusion, a full bladder allows the base of the prostate to be clearly seen, which allows for better visualization of the prostate. However, according to the authors, clinical practice shows that the bladder should not be overly distended, as this could lead to urinary incontinence during the biopsy procedure.

TRUS evaluation of the prostate begins with a systematic scan in the transverse or semicoronal plane, starting at the level of the seminal vesicles adjacent to the base of the prostate and continuing to the apical level, which visualizes the gland. areas. A sagittal plane examination is then performed to detect lobar asymmetry, as well as to confirm suspicious lesions detected on axial or coronal scans. The prostatic and extraprostatic structures evaluated using a systematic approach are listed in Table 1. Note that the ellipsoid formula allows the calculation of prostate size from diameters along orthogonal axes:

Anatomical structures assessed by TRUS

External gland

Internal gland

Anterior fibromuscular tissue

Capsule

Periprostatic adipose tissue

Periprostatic lymph nodes

Neurovascular bundles

Ejaculatory ducts

Seminal vesicles

Rectal wall

Urethra

In patients diagnosed with prostate cancer, an assessment of prostate size may be necessary to prescribe appropriate treatment. Proper assessment may also be helpful in the treatment of patients with undiagnosed cancer, as it can guide treatment for patients with symptoms of lower urinary tract obstruction. The transrectal ultrasound approach to the prostate also allows the operator to perform a variety of diagnostic and therapeutic interventions for prostate cancer due to its significantly higher accuracy than other ultrasound methods.

## **PROSTATE CANCER**

PCa is the second leading cause of cancer death in men. In addition to being a major medical problem, this disease also constitutes a significant public health problem due to its high economic costs. Although early detection of the disease is important for adequate treatment, small foci of cancer can be discovered in addition to large tumor lesions. Today, the main tools used to diagnose the disease are digital rectal examination, serum prostate-specific antigen (PSA) levels, and TRUS-guided prostate biopsy. Currently, the positive predictive value of prostate biopsy based on digital rectal examination, PSA, and TRUS results is low and leads to a significant number of unnecessary biopsies. Therefore, there is a clear need to improve the accuracy of prostate cancer diagnostic methods.

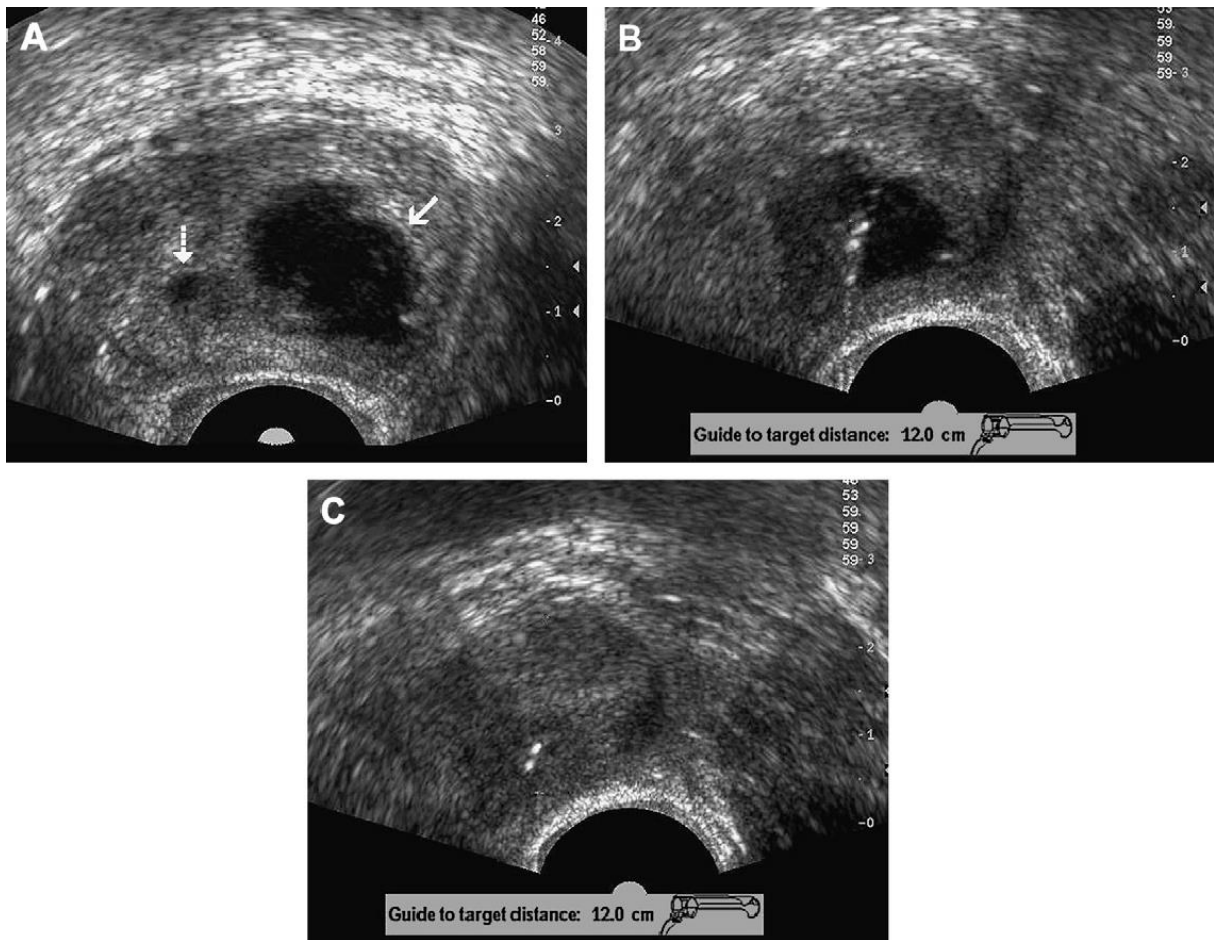
The most common indication for prostate ORTR is the diagnostic evaluation of suspected prostate cancer. Early detection of prostate cancer appears to be closely related to reduced mortality, as detection in early stages of the disease is often the only chance for treatment. Before diagnostic tools such as digital rectal examination, TRUS, and PSA tests were widely introduced to detect disease at an early stage, prostate cancer was often diagnosed at an advanced stage, leading to earlier death of patients. Although a total serum PSA (TSPS) level greater than 4 ng/mL may indicate the presence of prostate cancer, patients with BPH and inflammatory prostate disease may also have elevated total serum PSA levels. The lack of specificity of serum total PSA for CaP screening has inevitably led to further efforts to identify an ideal protocol combining PSA, TRUS, and digital rectal examination to improve specificity without compromising sensitivity. Although TRUS is recognized as the best ultrasound guidance method for biopsies, its low positive predictive value in the diagnosis of malignancies is a significant drawback.

TRUS technology has undergone constant improvements since its first clinical introduction in the 1960s. Although there is a consensus on the use of TRUS to assess prostate size and ultrasound for biopsy, its limited value for accurate detection of early-stage PCa and detection of local tumor spread still precludes its use, raising the main clinical question about its effectiveness. However, grayscale ultrasound can clearly define the zonal anatomy of the prostate, and the gland can be easily distinguished from periprostatic tissue, including the rectum, neurovascular bundles, and adipose tissue, by TRUS.

Classically, a hypoechoic lesion in the peripheral zone may indicate a malignant process, but CaP may have less isoechoic or hyperechoic features.

Prostate cancer. Transverse grayscale TRUS image shows an ill-defined, slightly hypoechoic mass in the subcapsular area (arrow) of the left lobe, histologically confirmed as an adenocarcinoma.

(A) Transverse gray-scale TRUS image with no obvious lesion in the peripheral zone. (B) Transverse TRUS color Doppler image of the same patient shows an area of vascular enhancement in the right peripheral zone (arrow), which was the only feature of a histopathologically identified adenocarcinoma. The tumor was invisible on gray-scale TRUS due to its isoechoic nature.



Currently, the use of other less specific features is necessary for the diagnosis of prostate cancer, since a significant proportion of detected prostate cancers are isoechoic. In this context, the following features may be useful: asymmetry, echotexture or glandular margin. Accordingly, a nonspecific irregular echo or a bulging or discontinuous capsule contour may indicate the presence of PCa. However, approximately half of PCa lesions are not visible on grayscale ultrasound. In addition, some types of pathology, e.g.: BPH, prostatitis, atrophy, hematoma, ductal ectasia and intraepithelial neoplasia can mimic the image of prostate cancer on grayscale ultrasound. Another challenge for the assessment of PCa is that it is mainly multifocal; a single circular formation can also occur, but this pattern is less common. Morphologically, only 30% of CaPs can present as a solitary nodule, a lesion with an infiltrative component occurs in about 50% of patients, and the infiltrative pattern predominates in the remaining 20%. Ultrasound shows advanced prostate cancer with a diffuse and heterogeneous hypoechoic peripheral echotexture, isoechoic or hyperechoic compared to normal prostate tissue.

### PROSTATE ULTRASOUND:

Prostate cancer. (A) Transverse grayscale TRUS image shows a round, hypoechoic mass located in the right peripheral zone (arrow). Neither color (B) nor power (C) Doppler TRUS revealed significant increased blood flow, predicting the neovascularization feature of PCa. (D) Transverse TRUS image illustrates the trajectory of the needle used to obtain a biopsy specimen from the lesion noted above.

Prostate cancer. (A, B) Transverse and longitudinal gray-scale TRUS images depicting a nodule located in the right peripheral zone (arrows in A and B). (C, D) Transverse and longitudinal TRUS Doppler images (arrows C and D) revealed vascular enhancement of the lesion.

Prostate cancer. (A) Transverse gray-scale TRUS image shows diffuse heterogeneous parenchymal echotexture with irregular capsular contour and prominent posterior extracapsular extension. The lesion has a significant protrusion and is located close to the rectal wall, indicating infiltration of cancer tissue. Transverse color (B) and power (C) TRUS Doppler images show increased blood

supply to the affected area. (D) Whole-body scan of the same patient shows multiple areas of increased growth in the axial skeleton, representing abnormal osteoblastic activity and consistent with a metastatic lesion.

Small cancers usually have a hypoechoic appearance, while tumor extension may result in an isoechoic lesion or a heterogeneous echogenic lesion. There are no specific sonographic features of transition zone cancers, but they differ from peripheral zone cancers in that they are clinically less aggressive. Therefore, routine biopsy is the only way to detect transition zone cancer. The concomitant presence of BPH may be a limiting factor in TRUS evaluation of the prostate, as its mixed signal reflection or peripheral compression effect may obscure prostate cancer.

In addition to adenocarcinoma, the most common histologic type of prostate cancer, sonographic features of rare prostate tumors have also been described. An adenomatous cyst of the prostate may appear with several identical small cysts. Comedocarcinoma, the most dangerous form of PC, appears sonographically as a hypoechoic area of cancer interspersed with numerous small heterogeneous hyperechoic foci. Lymphoma, on the other hand, has an ultrasound appearance of large hypoechoic masses in the transitional and peripheral zones. In summary, soft tissue masses that invade the bladder and prostate may present as rhabdomyosarcoma, which develops during childhood.

Although the use of TRUS in the diagnosis of PCa is limited, some TRUS findings can detect extracapsular extension. These findings include local protrusion or irregularity of the prostatic capsule and hypoechoic lines in the plane of periprostatic fat tissue. However, TRUS cannot detect extracapsular spread of small microscopic clusters of tumor cells.

## **COLOR DOPPLEROGRAPHY**

Doppler ultrasound is a tool for assessing local blood flow, which is closely related to tissue function and vitality. In color Doppler, the color palette is related to the direction of blood flow and the direction of the sensor when receiving the signal, where the flow to the sensor is shown in red and the flow from the sensor is shown in blue. On the other hand, with the accelerated growth rate, the increased blood supply demand of cancer tissues is more obvious than that of normal tissues, which can lead to significant changes in local hemodynamics. As a result, this affects the ability to see and detect cancer using color Doppler ultrasound. An increase in the number of dilated and atypical blood vessels, reflecting angiogenesis and increased blood flow in tumor tissue, can be detected by color Doppler ultrasound. Technically, increased blood flow can be demonstrated by spectral analysis using pulsed wave Doppler, which detects waves representing changes in frequency or speed, or color Doppler, which shows a spectrum of colors representing the average range of changes in frequency or speed of red blood cells in the bloodstream.

Previously, color Doppler ultrasound was thought to be the best diagnostic for prostate cancer, as it allowed to determine the diffuse, local, and surrounding nature of blood flow. It was later determined that the technique had low specificity for proper assessment. In addition, hypoechoic lesion and hypervascularity suggestive of Ca are not correlated. However, color Doppler signal has been shown to correlate well with PCa stage and type, as well as with the risk of recurrence after treatment, which is essential to determine the behavior and aggressiveness of PCa. Consequently, color Doppler ultrasound has been useful in distinguishing low-risk hypovascular tumors from high-risk hypervascular tumors, since the latter group is associated with hypervascularity and represents a higher Gleason tumor stage, which is an extraprostatic tumor "implies a high risk." of Simta enlargement. Targeted biopsy relies solely on high-frequency color or power Doppler imaging, as there is theoretically a risk of missing a significant number of tumors. In addition to quantifying blood flow, color Doppler ultrasound can calculate microvascular density (distribution of microvessels), which can be useful for assessing blood flow in the prostate. Naturally, microvessel density was higher in metastatic tumors, which is typical of PCa. Since biopsy underestimates Gleason histology, microvessel density can be used as an indicator of disease prognosis. Technical limitations of color Doppler imaging for prostate assessment include the

angular dependence of Doppler flow, intraprostatic noise that mimics flow enhancement, and inadequate detection techniques at low flow rates.

## POWER DOPPLEROGRAPHY

Power Doppler has less angle dependence than color Doppler and provides information on the presence and intensity of flow signals. The advantage of this technique is to detect slow flow in small tumor vessels and even subtle changes in blood flow. However, it is not possible to predict the direction of flow with this method. Power Doppler ultrasound, which has a 3- to 4-fold higher sensitivity for detecting prostate cancer, also helps in the differential diagnosis of BPH and prostate cancer. However, this technique has rarely been shown to be superior to color Doppler in detecting PCa. Although power Doppler can help determine an appropriate site for prostate biopsy by identifying areas of local hypervascularity, it is not considered superior to color Doppler and is useful for targeted biopsy only if the number of biopsies throughout the prostate is limited. Combined grayscale ultrasound and TRUS color Doppler-guided biopsy are not sensitive enough to obviate the need for routine biopsy. A recent study showed that spectral waveform measurement of the prostatic capsular and urethral arteries using power Doppler ultrasound may be useful in distinguishing prostate cancer from benign hypertrophy. Researchers also hypothesized that increasing the number of biopsies limited to abnormal spectral Doppler index values would increase the diagnostic efficiency in detecting PCa.

### Liste de la littérature utilisée:

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 AH 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., & Исмойлов, 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 кератоувеитов 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., Ahmedov, 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 БЕМОРАЛДАРДА БУРУН БЎШЛИГИ МУКОЦИЛИАР ТРАНСПОРТИ НАЗОРАТИ ТЎҒРИСИДАГИ ЗАМОНАВИЙ ҚАРАШЛАР (адабиётлар шархи). 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. Т [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).