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Potential use of radiation methods for diagnosing bone metastases of castration-resistant prostate cancer: a literature review

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ABSTRACT

Metastatic castration-resistant prostate cancer (mCRPC) is the tumor progression with the development of resistance to androgen deprivation therapy. The incidence of bone metastases in these patients reaches 90%. Radiology is widely used to diagnose mCRPC. Computed tomography (CT) and magnetic resonance imaging (MRI) are beneficial in anatomic imaging, but have some limitations in evaluating effectiveness of disease treatment. Scintigraphy is used to screen for bone metastases, but is poorly suited for assessing disease progression. Positron emission tomography (PET) combined with CT and single-photon emission CT are used for early detection of local or systemic spread of prostate cancer. PET of prostate-specific membrane antigen is used to predict the effectiveness of anti-tumor therapy based on the absorbed dose of a radiopharmaceutical (RP). The introduction of RPs (^{177}Lu-PSMA) opens up new perspectives for radionuclide therapy with simultaneous evaluation of its efficacy using hybrid visualization. The potential use of radiology in the diagnosis of bone metastases is of particular interest for the analysis and systematization of the data obtained and for the development of indications for radioligand therapy and the evaluation of its efficacy.

Published data indicate that radiologic modalities for the diagnosis of mCRPC vary in sensitivity and specificity and have their own advantages and limitations, so these modalities should be combined.

The development and improvement of methods to quantitatively assess treatment efficacy and identify prognostic markers will enable more informed selection of treatment strategies and radiopharmaceuticals, leading to improved overall survival.

Keywords: prostate cancer; bone metastases; single-photon emission computed tomography; positron emission tomography; magnetic resonance imaging; multislice computed tomography; radiomics.

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Возможности лучевых методов диагностики метастазов в кости кастрационно-резистентного рака предстательной железы (обзор литературы)

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АННОТАЦИЯ

Метастатический кастрационно-резистентный рак предстательной железы (мКРРПЖ) — это прогрессирование опухолевого процесса при формировании невосприимчивости к андроген-депривационной терапии. Частота появления метастазов в костях у таких пациентов достигает 90%. В диагностике мКРРПЖ широко используют лучевые методы исследований. Компьютерная томография и магнитно-резонансная томография обладают преимуществами в анатомической визуализации, однако имеют ограничения в оценке эффективности лечения заболевания. Сцинтиграфию применяют для скрининга метастатического поражения костей скелета, но при этом затруднён анализ прогрессирования заболевания. Позитронно-эмиссионную томографию (ПЭТ), совмещённую с компьютерной томографией, и однофотонную эмиссионную компьютерную томографию используют для раннего выявления местного или системного распространения рака предстательной железы. Информация о количестве поглощённого радиофармпрепарата (РФП) с помощью ПЭТ-визуализации простатоспецифичного мембранного антигена используют для прогнозирования эффективности противоопухолевой терапии. С внедрением в практическую деятельность РФП (^{177}Lu-PSMA) открылась перспектива проведения радионуклидной терапии с одновременным определением её эффективности методами гибридной визуализации. Возможности методов лучевой диагностики метастазов в кости представляют особый интерес для изучения и систематизации получаемых данных и разработки показаний для проведения радиолигандной терапии и анализа её эффективности.

Опубликованные данные свидетельствуют о том, что лучевые методы диагностики мКРРПЖ обладают различной чувствительностью и специфичностью, имеют свои преимущества и недостатки, что говорит о необходимости комплексного подхода в их использовании.

Разработка и развитие методик количественной оценки эффективности лечения, выявление прогностических маркёров позволит грамотно выбрать необходимую тактику лечения и облегчит подбор РФП, что приведёт к увеличению общей выживаемости.

Ключевые слова: рак предстательной железы; костные метастазы; однофотонная эмиссионная компьютерная томография; позитронно-эмиссионная томография; магнитно-резонансная томография; мультиспиральная компьютерная томография; радиомика.

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放射方法诊断去势抵抗性前列腺癌骨转移的可能性（文献综述）

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摘要

转移性去势抵抗性前列腺癌（mCRPC）是一种对雄激素剥夺疗法形成耐药性的肿瘤发展阶段。此类患者骨转移的发生率达90%。放射方法广泛用于mCRPC的检查。计算机断层扫描和磁共振成像在解剖成像方面具有优势，但在疾病疗效评估方面存在局限性。闪烁扫描法用于筛查转移性骨骼病变，但很难分析疾病的进展情况。正电子发射计算机断层扫描（PET）结合计算机断层扫描和单光子发射计算机断层扫描可用于早期检测前列腺癌的局部或全身扩散。前列腺特异性膜抗原PET成像中放射性药物吸收量的信息，可用于预测抗癌治疗的效果。随着放射性药物 （177Lu-PSMA） 在实践活动中的推广，开辟了混合成像方法同时确定其疗效的放射性核素疗法的前景。骨转移放射诊断方法的可能性对于研究和系统化所获得的数据、研究放射配体治疗的适应症和分析其疗效具有特别重要的意义。

已发表的数据证明，用于诊断mCRPC的放射方法具有不同的敏感性和特异性，并且各有优缺点，这表明在使用这些方法时需要采取综合方法。

定量评估治疗方法、预后标志物判定的研究和发展，可以正确的选择必要的治疗策略，并简化放射性药物的选择，从而提高总体存活率。

关键词：前列腺癌；骨转移；单光子发射计算机断层扫描；正电子发射计算机断层扫描；磁共振成像；多螺旋计算机断层扫描；放射组学。

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INTRODUCTION

Prostate cancer (PC), one of the most prevalent cancers in men, originates in the glandular epithelium of the prostate [1]. From 2011 to 2021, the incidence of PC in Russia rose by 41.69% [2], making it a socially and economically significant concern. The development of metastatic castration-resistant PC (mCRPC), which is caused by a proliferation of androgen-insensitive cells, makes resistance to androgen deprivation therapy particularly significant [3]. The mean time to hormone therapy resistance is 1.5–2 years, which limits future therapeutic choices. This is complicated by significant variability in tumor morphology, serum prostate-specific antigen (PSA) levels, disease stage, and the risk of relapse [4].

The prognosis worsens with metastatic disease, with only 30% of patients surviving for five years [5]. The incidence of bone metastases in patients with mCRPC can reach 90% [6]. Visceral metastases are most frequently observed when secondary bone lesions are already present, which suggests a poor prognosis [7].

The initial development of bone metastases is determined by an imbalance between bone-resorbing cells (osteoclasts) and bone-forming cells (osteoblasts) resulting from interactions between cancer cells and elements of the internal bone milieu [8, 9].

Diagnostic imaging techniques are essential for the initial assessment of the tumor grade and the number and size of metastases, as well as for monitoring patients with mCRPC during treatment. Each diagnostic radiology technique has its own advantages and limitations. Multislice computed tomography (MSCT) and magnetic resonance imaging (MRI) effectively detect advanced tumors owing to anatomical imaging; however, their application in assessing PC treatment efficacy is restricted. Scintigraphy performs well in screening for bone metastases because of its high sensitivity, but is less effective in evaluating disease progression [10].

For the early detection of local or systemic tumors in PC, hybrid diagnostic techniques like positron emission tomography with computed tomography (PET/CT) and single-photon emission computed tomography with computed tomography (SPECT/CT) with diagnostic radiopharmaceuticals are utilized, taking into account the functional and morphological components of the obtained data [11].

Prostate-specific membrane antigen (PSMA) ligand PET has significantly augmented diagnostic algorithms for patients with PC owing to quantitative data on radiopharmaceutical uptake in the targeted areas. Though there are some unresolved concerns, PSMA PET/CT has demonstrated promising results in predicting the efficacy of cancer treatment [12].

Radionuclide therapy in mCRPC targets PSMA, with subsequent imaging examinations to confirm radionuclide binding [13]. Early relapses, high serum PSMA levels, Gleason scores, and a more aggressive illness are all correlated with PSMA expression [14, 15].

Physiologically, PSMA is also expressed in the lacrimal and salivary glands, proximal renal tubules, liver, spleen, and proximal small intestine [14]. The presence of PSMA activity has been documented in the peripheral ganglia and central nervous system [16].

The most promising and frequently used isotopes for radioligand therapy are ^{177}Lu and ^{225}Ac. ^{177}Lu has unique diagnostic and therapeutic benefits, including the binding of PSMA molecules by β– and γ-emitters ^{177}Lu-PSMA. ^{225}Ac exerts a powerful therapeutic effect via binding of PSMA by the α-emitter ^{225}Ac-PSMA [3]. Prostate tumor cells accumulate ^{225}Ac- or ^{177}Lu-labeled PSMA ligands, which damages DNA and eventually results in tumor cell death [17, 18].

Clinicians treating PC should focus on defining objective patient selection parameters for radioligand therapy, as well as on the early detection and imaging assessment of relapses following various PC therapies.

This review examines the potential of various diagnostic radiological modalities in mCRPC patients.

DIAGNOSTIC RADIOLOGY TECHNIQUES

Radiography is an imaging technique that generates consolidated images of organs, bone structures, and tissues employing the penetrative properties of X-rays. It is a reliable and accessible method for evaluating the structure and location of bone metastases [19]. Kitagawa et al. [20] revealed that radiography exhibits high specificity (80.9%), low sensitivity (45.8%) [due to limited contrast uptake by bone marrow lesions], and an accuracy of 74.8% [20]. If the bone matrix loss is less than 25%–30%, it is difficult to detect bone metastases early by radiography; also, there is limited ability to evaluate medulla alterations [21]. Thus, conventional radiography techniques are more effective for the urgent detection of fractures and postoperative monitoring of surgical hardware and implants [21].

Multislice CT (MSCT) is a modern diagnostic radiology technique that uses X-rays to generate cross-sectional images. Because of its high resolution, MSCT produces detailed organ and tissue images. In a meta-analysis examining the diagnostic utility of diagnostic radiology modalities in patients with spinal metastases, the sensitivity and specificity of MSCT were 79.2% and 92.3%, respectively [22–24].

One of the primary benefits of MSCT is the short scan time, which is especially essential in emergency circumstances where patients suddenly develop pain. This technique identifies fractures caused by existing secondary bone lesions and spinal nerve compression [21, 23]. However, due to the limited contrast uptake by soft tissues, MSCT is seldom used as a primary diagnostic tool in PC. It is more typically employed for the detection of distant metastases and for biopsy guidance [19]. This technique determines

the structure of the bone metastases and the extent of bone destruction. Additionally, it enables the use of extra image processing techniques for metal artifact reduction in the imaging-based evaluation of surgical hardware [23]. The formation of reactive sclerosis during treatment and the progression of osteoblastic metastases appear to be similar on MSCT scans (by increased lesion density). Because of this characteristic of bone metastases, the RECIST 1.1 criteria categorize these lesions as non-measurable (Fig. 1) [24]. Radiomics facilitate the quantitative assessment of lesions [25].

Magnetic resonance imaging is a diagnostic radiological modality that generates images using electromagnetic waves in a constant magnetic field. The advantages of MRI include the lack of ionizing radiation and superior soft tissue imaging. It is one of the most effective techniques for noninvasive bone marrow evaluation (Fig. 2). In addition to anatomical diagnosis, MRI is useful in determining the degree of spinal stenosis and compression, the size and location of lesions, and the extent of vascular supply [23]. The disadvantages include a lengthy scan time and a variety of contraindications, such as the presence of pacemakers and metal implants [26, 27].

A multiparametric approach to the diagnosis of mCRPC involves the evaluation of anatomical T1-weighted images (T1WIs) (scar tissue identification for evidence of replacement fibrosis) and T2WIs (for edema detection) for a detailed examination of the anatomical zones of the prostate and surrounding soft tissues. Short tau inversion recovery sequences, which eliminate the influence of fluid in the resulting images, can be used to differentiate between fat and fluid inclusions in the lesions. Functional diffusion-weighted imaging (DWI) sequences with apparent diffusion coefficient maps may be employed to determine tumor location and aggressiveness. Dynamic contrast-enhanced MRI is utilized for differentiating between inflammatory and benign changes, as well as for ascertaining tumor location and grade [28].

In a prospective study by Perez-Lopez et al. (TOPARP-A) [29], a whole-body DWI MRI was performed in 21 patients with bone metastases at baseline and 12 weeks following treatment. Out of all the bone metastases, five lesions were selected and evaluated. The volume and diameter of the lesions declined 12 weeks after olaparib therapy; the outcomes were inversely proportional to the treatment response. The authors concluded that DWI can play a critical role in assessing the response of bone metastases to mCRPC treatment.

The published results of studies comparing bone scintigraphy and whole-body MRI varies, most likely because different MR scanners are used and there are no established protocols. A meta-analysis revealed that whole-body MRI exhibits a higher sensitivity and specificity (94% and 99%, respectively) than bone scintigraphy (80% and 95%, respectively), indicating that whole-body MRI can be used to verify or rule out bone metastases [30, 31].

Padhani et al. [32] developed and presented guidelines (MET-RADS-P) for whole-body MRI efficacy criteria to assess

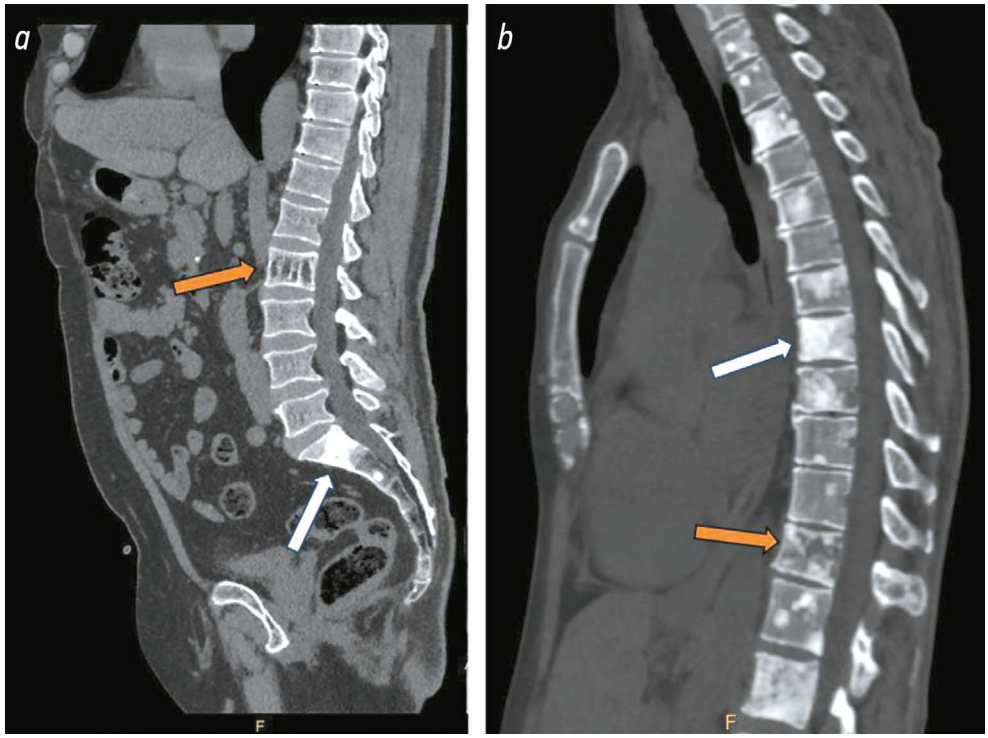

Fig. 1. *a*, Lumbar spine MSCT, sagittal plane: osteoblastic lesions observed in the S1 and S2 vertebral bodies (white arrow), hemangioma in the L2 vertebral body (orange arrow); *b*, thoracic spine MSCT, sagittal plane: osteoblastic lesions in thoracic vertebral bodies (white arrow), mixed lesion noted in the Th12 vertebral body (orange arrow).

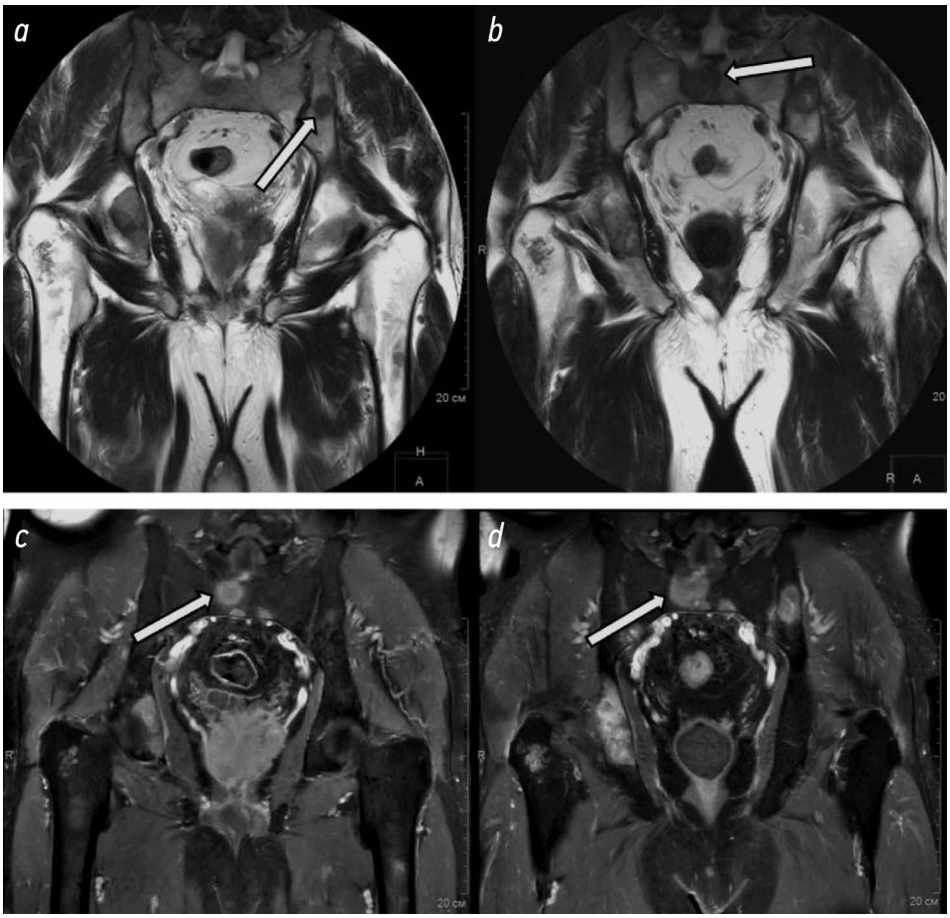

Fig. 2. *a*, *b*, Pelvic MRI, coronal plane, T2WI; *c*, *d*, pelvic MRI, coronal plane, T1WI; case follow-up *a*, *c* of February 2023 and *b*, *d* July 2023: osteoblastic lesions in pelvic bones, increase in lesion size during follow-up (white arrows).

lesions in patients with advanced PC. According to the authors, accurate assessment of the response to treatment will facilitate the future development of targeted therapy [27].

Due to radiopharmaceutical absorption, hybrid diagnosis techniques are more successful in determining the functional state of lesions than anatomical imaging and bone metastasis follow-up using MSCT and MRI [26].

Bone scintigraphy is a radionuclide imaging technique that utilizes diphosphonate complexes to examine bone lesions. The technique entails assessing the radiopharmaceutical uptake involved in bone metabolism at active bone formation sites, which are linked to benign and malignant abnormalities, as well as physiological processes [24]. In posttraumatic, neoplastic, and infectious alterations, radiopharmaceutical uptake is correlated with local blood flow and osteoblast/osteoclast activity [33].

When activity is identified in the scintigrams of patients with bone metastases, the 2 + 2 rule is used to account for the flare phenomenon detected during osteoblast activation and sclerotic transformation of lesions in the early treatment period [34]. The emergence of two new lesions at a follow-up imaging test six weeks or more after the initial diagnosis is considered progression. An increase in the size of the lesions detected on bone scintigraphy is not regarded as a sign of disease progression [35]. Since this phenomenon is identified within the first three months following chemotherapy and hormone therapy, it may resemble disease progression [36].

Of significance are the scintigram quantitative assessment parameters, such as the bone scan index (BSI) and bone scan lesion area (BSLA).

BSI is the sum of individual bone areas multiplied by the percentage of each bone's involvement in metastasis. Processing BSI values manually or semiautomatically is time-consuming and subjective. Therefore, scintigram assessment techniques using aBSI automated computer analysis were developed [37, 38], which significantly increase the reproducibility of quantitative assessment to 10 s as opposed to 5–30 minutes with manual assessment [39]. When combined with the diagnostic evaluation of anatomical images, aBSI parameters can be utilized as prognostic biomarkers.

Dennis et al. [40, 41] assessed preliminary data and discovered that BSI changes during treatment were closely correlated with overall survival in patients receiving chemotherapy. The evaluation was carried out three to six months following treatment. The authors concluded that a twofold increase in BSI during treatment results in a 1.9-fold increased risk of death.

Bone scintigraphy enables the detection of early metabolic changes, frequently several weeks or months

before they are detected by radiography. Given that the sensitivity and specificity of this technique for detecting bone metastases in PC are 74.5%–83% [42–44] and 62%–82%, respectively, the use of complementary anatomical imaging approaches, such as radiography, MSCT, MRI, or hybrid methods (SPECT/CT and PET/CT) is required [34].

After comparing bone scintigraphy and MRI findings [44], the authors concluded that bone scintigraphy is a rapid and cost-effective technique for the early detection of bone metastases. However, there are several limitations, including the accumulation of radiopharmaceutical agents in inflammatory lesions and regions of intensive bone formation. Lytic bone lesion imaging is challenging due to the lack of bone remodeling and the presence of a soft tissue component where radiopharmaceutical uptake is not feasible [12].

This method can be supplemented by SPECT/CT findings. An additional benefit is the use of BSI as a prognostic marker. The limitations of bone scintigraphy include reduced potential for imaging of lytic lesions (only lesions with radiopharmaceutical uptake can be assessed), lengthy scan time, lower sensitivity compared to CT and MRI, and the flare phenomenon in response to treatment [27, 33].

An additional SPECT/CT can help avoid these limitations.

Single-photon emission computed tomography with computed tomography is a hybrid diagnostic radiology technique that generates 3D images using a gamma chamber and a multislice CT scanner. After computer processing, maps with functional information on metabolic processes in various organs and tissues were matched with anatomical CT images [45]. This approach reduces the disadvantages of each method and improves the diagnostic value.

SPECT/CT results are used to semi-quantitatively assess lesions using the standardized uptake value body weight (SUVbw), a parameter based on body weight. The following formula is used for differentiating between degenerative changes and metastatic lesions:

$$SUVbw = \frac{A \times B}{C},$$

where A = local activity concentration, B = body weight, and C = administered activity. SUV_{bw} values in bone metastases are significantly higher than in degenerative changes; the sensitivity and specificity in differential diagnosis are 73.8% and 85.4%, respectively [46, 47].

The diagnostic utility of scintigraphy with ^{177}Lu-PSMA was assessed in patients with PC with elevated PSA levels and negative findings on conventional imaging examinations (MSCT, MRI) [48]. The analysis included 26 patients with PSA failure after curative therapy; ^{177}Lu-PSMA was administered, and SPECT/CT and whole-body planar scintigraphy were then performed. According to SPECT/CT findings, the total metastasis detection rate was 38.5%, with secondary lesions being most frequently detected in the lungs, abdominal lymph nodes, and mediastinum. When PET/CT with ^{68}Ga-PSMA

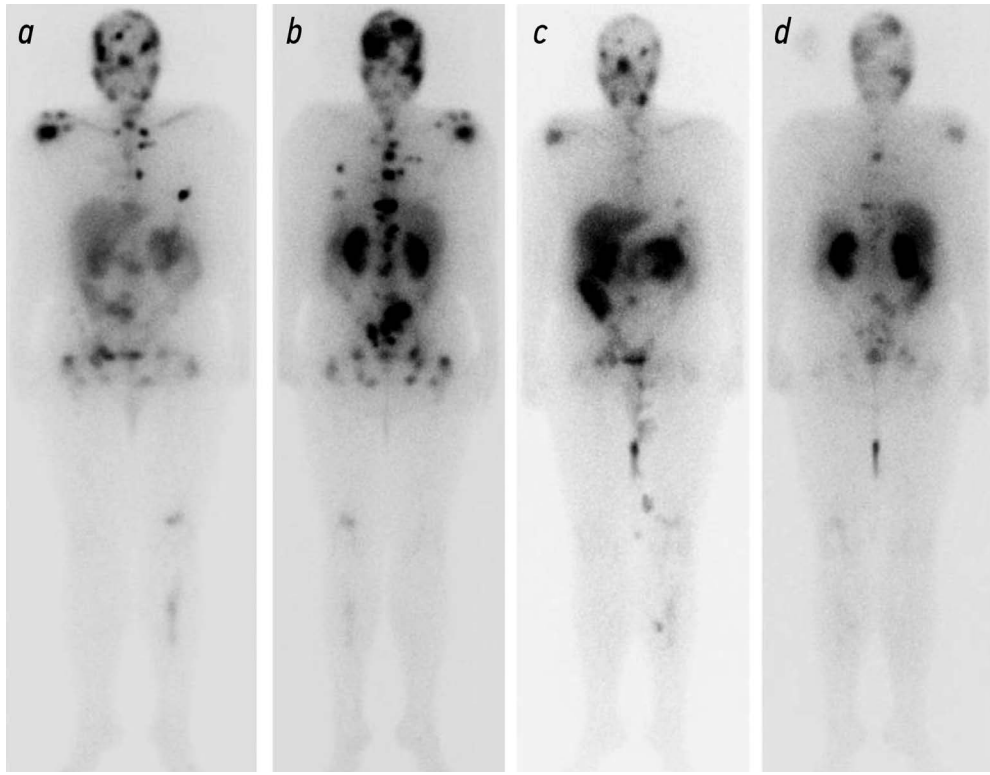

Fig. 3. *a*, Whole-body scintigraphy with ^{177}Lu-PSMA, anterior view; *b*, posterior view of December 2021: diffuse-plus-focal radiopharmaceutical hyper uptake of differing intensity, multiple PSMA-positive bone lesions; *c*: whole-body scintigraphy with ^{177}Lu-PSMA, anterior view; *d*, posterior view of April 2022: reduced radiopharmaceutical uptake in the lesions, absence of new areas of radiopharmaceutical hyper uptake.

is unavailable, SPECT/CT with ^{177}Lu-PSMA can detect secondary lesions in more than one-third of patients, making it a valuable diagnostic tool in mCRPC patients (Fig. 3).

Several authors have conducted comparative studies of SPECT/CT and MRI. When assessing the potential of SPECT/CT and whole-body MRI in patients with bone metastases, the sensitivity, specificity, and precision of both methods were found to be 94.4%, 75%, and 92.3%, respectively, indicating that these modalities are complementary (Table 1) [23, 49, 50].

Positron emission tomography with CT is a hybrid radionuclide diagnostic method that makes use of a three-dimensional distribution of radio-emitting indicators labeled with positron (β^+) emitters. This enables the noninvasive assessment of the body's biochemical and functional processes [45]. PET/CT uses radiopharmaceuticals such as ^{18}F-FDG (fluorodeoxyglucose) and amino acid-based agents to detect diverse molecular and cellular mechanisms of tumor metabolism [45].

Semiquantitative measurements and the standardized uptake value (SUV) allow for the differentiation of malignant and benign lesions [51].

The use of ^{18}F-FDG PET/CT in the initial assessment and PC staging is restricted. This approach is not recommended for detecting bone metastases in patients with PC. Low bone tissue glucose consumption and inadequate ^{18}F-FDG uptake make it difficult to identify osteoblastic lesions. Moreover, this approach does not distinguish between primary and secondary lesions, particularly for small lesions [45].

^{18}F-NaF (sodium fluoride) is a positron emitter that binds to osteoblasts during osteogenesis, producing positive findings in both benign and malignant lesions [51].

In PC, proliferating tumor cell membranes contain ^{18}F-CH (fluorocholine) [52]. ^{18}F-CH exhibits a longer half-life than ^{11}C-choline (up to 109.8 minutes vs. 20.4 minutes), making it appropriate for PET centers without a cyclotron and increasing its availability. Compared to ^{18}F-FDG, this agent was reported to be more successful in detecting metastases in PC because of greater radiopharmaceutical uptake in bone lesions [53].

When analyzing the PET/CT findings in patients with bone metastases, ^{18}F-CH and ^{18}F-NaF demonstrated comparable sensitivity of 91%. However, the specificity of PET/CT with ^{18}F-CH and ^{8}F-NaF was 89% and 83%, respectively [54].

PET/CT identifies metabolic changes before the detection of morphological changes by MSCT. ^{18}F-CH PET/CT is comparable to whole-body MRI and superior to bone scintigraphy and MSCT. However, it is linked to disadvantages such as the flare phenomenon, inadequate liver and urinary tract imaging, and inconsistent detection of small lesions at low serum PSA levels [27].

The effectiveness of antineoplastic treatment can be predicted using quantitative data on radiopharmaceutical uptake provided by PSMA PET.

The FDA approved ^{68}Ga-PSMA and ^{18}F-PSMA in 2020 and 2021, respectively, as the first and second PSMA PET indicators for patients with PSA failure [55].

According to the working group guidelines (PCWG3, 2016), the evaluation of baseline data and follow-up in patients with PC must be based on diagnostic radiological findings [43]. The RECIST 1.1 criteria for anatomical imaging must be used to solid tumors identified by MSCT and MRI [56], whereas the response criteria (PERCIST) must be used to evaluate PET/CT results [57].

Anatomical imaging methods along with serum PSA measurement are used to evaluate therapy response for solid tumors in PC patients based on the RECIST criteria [58].

According to the PERCIST criteria, the response to treatment is assessed qualitatively (e.g., based on the presence/absence of lesion activity) and quantitatively, where the initial and follow-up imaging parameters must be identical. The standardized uptake value normalized by lean body mass (SUL) is used for measurements. The results are presented as a percentage of the peak SUL for the lesion exhibiting the highest activity [59].

Table 1. Comparison of the diagnostic criteria for bone lesion detection employing diagnostic radiological techniques

Diagnostic method	Study (publication)	Patients/studies, n	Sensitivity, %	Specificity, %
Radiography	Kitagawa et al., 2018 [20]	129	45.8	80.9
MSCT	Liu et al., 2017 [22]	183 (3)	79.2	92.3
MRI	Liu et al., 2017 [22]	381 (7)	94.1	94.2
	Sun et al., 2020 [31]	1939 (15)	94	99
SPECT/CT	Sun et al., 2020 [31]	1939 (15)	80	95
	Sheikhbahaei et al., 2019 [42]	507 (14)	79	62
	Shen et al., 2014 [43]	901 (12)	83	82
ОФЭКТ/КТ	Liu et al., 2017 [22]	343 (4)	90.3	86
	Mohd Rohani et al., 2020 [46]	34	73.8	85.4
ПЭТ/КТ	Liu et al., 2017 [22]	403 (5)	89.8	63.3

Maffey-Steffan et al. [58] compared the findings of ^{68}Ga-PSMA PET/CT (interpreted using modified PERCIST criteria, with a semiquantitative SUVmax analysis) and whole-body ^{177}Lu-PSMA scintigraphy performed 24 hours after treatment, using the tumor-to-background ratio. Progression was defined as the emergence of new lesions and/or increased radiopharmaceutical uptake, partial remission as the elimination of one or more lesions and/or decreased radiopharmaceutical uptake, and stable disease as no changes in the number of lesions and radiopharmaceutical uptake. A mixed response was characterized by the elimination of some lesions and/or their decreased radiopharmaceutical uptake, with the emergence of new lesions. The results matched the visual perception of various imaging methods. The interpretation of 24-hour SPECT/CT findings is sufficiently accurate, and the technique is simple and cost-effective. Follow-up PET/CT is time-consuming, making examinations in patients with pain syndrome challenging. For monitoring patients, the PSA level must be measured and 24-hour SPECT/CT findings must be analyzed, whereas PET/CT should be utilized for patient selection and treatment efficacy assessment [59].

The LifeX software was used for assessing ^{68}Ga-PSMA PET/CT images, including the analysis of PSMA levels and their expression in the tumor, with a prespecified SUV threshold of 3.0 (based on software settings) and 45% (based on published findings of previous studies). The resulting data were manually updated. A decline in tumor volume and PSMA expression after treatment was reported in 63% and 74% of patients, respectively; moreover, there were significant differences in SUV_{max} values before and after treatment. The authors concluded that a quantitative analysis of the molecular volume and PSMA expression in the tumor can be employed to assess the response to ^{177}Lu-PSMA therapy [57, 60].

Another study used ^{18}F-NaF PET/CT and ^{99m}Tc SPECT/CT to assess SUV_{max}, SUV_{peak}, SUV_{mean}, metabolic bone volume, and total bone uptake. The formula $SUV_{mean} \times MBV$ was applied for each lesion with radiopharmaceutical uptake. The preliminary conclusion was that SUV parameters with SPECT/CT were substantially lower than those with PET/CT. However, compared to PET/CT, the radiopharmaceutical uptake with SPECT/CT was significantly higher. The values of metrics calculated for metastatic lesions were significantly higher than those for benign lesions [61].

Vlachostergios et al. [62] compared ^{68}Ga-PSMA PET/CT with a quantitative assessment and SPECT/CT with a semiquantitative assessment in ^{177}Lu-PSMA therapy. Three lesions with the highest radiopharmaceutical uptake in comparison to the liver were evaluated using SPECT/CT results. A five-point scale was used, with 0 denoting no changes, 1 denoting low tumor activity, 2 denoting strong tumor activity but below that of the liver, 3 denoting tumor activity equal to that of the liver, and 4 denoting tumor activity greater than that of the liver. The PET/CT findings were then used to evaluate the average SUV_{max} for the five lesions with the greatest radiopharmaceutical uptake compared to the SUV_{mean} of the liver. The following scale was used: 0 = no changes, 1 = $SUV_{max} < SUV_{mean}$ of the liver, 2 = SUV_{max} = 1–2.5 × SUV_{mean} of the liver, 3 = SUV_{max} = 2.5–5 × SUV_{mean} of the liver, and 4 = $SUV_{max} > 5 \times SUV_{mean}$ of the liver. The authors found that semiquantitative PSMA measurements using SPECT/CT and PET/CT can serve as prognostic indicators of overall survival in patients with mCRPC because this parameter represents the metastatic load.

A study [63] assessed the efficacy of radioligand therapy with ^{177}Lu-PSMA in patients with mCRPC. A technique developed in Germany has shown a significant increase in the overall survival and quality of life. In a multicenter study, 145 patients received one to four rounds of ^{177}Lu-PSMA treatment, with an overall biochemical response of 45%. For patients with PSA failure, PSMA-based hybrid imaging greatly increases the diagnostic efficacy. PSMA PET/CT can be valuable in radiotherapy planning because it can identify affected lymph nodes and rule out distant metastases, resulting in treatment adjustments in up to 30% of patients. Radionuclide therapy with labeled PSMA analogs enhances the diagnosis and treatment of mCRPC, which needs to be validated in prospective studies.

A multicenter, retrospective study was conducted by a group of researchers [64] to establish a RECIP 1.0-based approach (PSA + RECIP) to standardize the criteria of response to ^{177}Lu-PSMA therapy based on PET/CT findings for treatment efficacy assessment in mCRPC. This study aimed to formulate an integrated response classification combining laboratory PSA levels and response criteria based on PET/CT findings. This approach incorporated the analysis of the PSMA-positive tumor volume (PSMA VOL) and the detection of new metastases, employing a standardized system to determine the response criteria.

This method yielded four response categories: RECIP-CR for complete response, RECIP-PR for partial response, RECIP-PD for disease progression, and RECIP-SD for stable disease.

The results achieved using the RECIP 1.0 approach (PSA + RECIP) included the following:

- Reduction in PSA levels by ≥50% or RECIP-CR/RECIP-PR;
- Rise in PSA levels by ≥25% or RECIP-PD.

The study assessed the predictive value of RECIP 1.0 in terms of increases in overall survival. However, these findings must be corroborated in prospective studies [64].

Like all diagnostic radiology techniques, PET/CT has limitations, including motion artifacts, which result in incorrect image matching, and truncation artifacts due to differences in the field of view of CT and PET scanners (50 cm vs. 70 cm), especially in patients with excess body weight. Another disadvantage is that when PET shows radiopharmaceutical uptake, no changes are observed on CT. The results of these examinations must be interpreted with caution [45].

Table 2. Comparison of the diagnostic radiological techniques

Diagnostic radiological technique	Bone tissue morphology	Bone tissue metabolism	Bone marrow lesions	Diffusion	Radiopharmaceutical metabolism
Radiography	■				
MSCT	■				
MRI			■	■	
Bone scintigraphy		■			
SPECT/CT		■			
PET/CT	■	■			■

Note. Highlighted: the parameter is present; not highlighted: the parameter is absent.

Table 2 presents a comparison of diagnostic radiological procedures based on the parameters that indicate the presence of bone metastases in PC (adapted from Isaac et al. [65]).

Thus, available evidence demonstrates the heterogeneity of data regarding the diagnostic utility and potential of diagnostic radiological techniques, which are essential for the noninvasive assessment of mCRPC.

CONCLUSION

There are multiple diagnostic radiological techniques and associated approaches for the quantitative assessment of mCRPC. These techniques are widely employed in mCRPC diagnosis and staging, as well as in treatment strategy selection and efficacy assessment. The advantages and disadvantages of imaging examinations in this patient population are considered complementary because of their differing sensitivity and specificity; thus, an integrated use of these techniques is recommended.

A review of published evidence suggests that radionuclide diagnosis and therapy with ^{177}Lu-PSMA and ^{225}Ac-PSMA can be a promising strategy. These radiopharmaceuticals offer unique opportunities for targeted therapy and quantitative assessment of ^{177}Lu-PSMA therapy efficacy through diagnostic radiological techniques.

Further development of quantitative efficacy assessment tools for mCRPC therapy and the identification of prognostic biomarkers using radionuclide imaging techniques will help select the optimal treatment strategy, thereby improving overall survival.

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REFERENCES

1. Kaprin AD, Alekseev BYa, Matveev VB, et al. Rak predstatel'noi zhelezy. Klinicheskie rekomendatsii // Obshcherossiiskii natsional'nyi soyuz «Assotsiatsiya onkologov Rossii». 2021. (In Russ.) EDN: RLCXWE

2. Gevorkyan AR, Molodtsov MS, Aleksandrov EV. Prostate cancer diagnosis as part of high-tech advanced outpatient medical care. *Urology Herald.* 2023;11(1):26–33. doi: 10.21886/2308-6424-2023-11-1-26-33

3. Ling SW, de Blois E, Hooijman E, et al. Advances in ^{177}Lu-PSMA and ^{225}Ac-PSMA Radionuclide Therapy for Metastatic Castration-Resistant Prostate Cancer. *Pharmaceutics.* 2022;14(10):2166. doi: 10.3390/pharmaceutics14102166

4. Sekhoacha M, Riet K, Motloung P, et al. Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches. *Molecules.* 2022;27(17):5730. doi: 10.3390/molecules27175730

5. Solodky VA, Pavlov AYu, Fomin DK, et al. Determination of the role of lutetium-PSMA in prostate cancer. *Vestnik RNTsRR.* 2022;22(2):27–36. EDN: UNNDSN

6. Medvedeva AA, Chernov VI, Usynin EA, et al. Use of ^{177}Lu-PSMA for radionuclide therapy in patients with castrate-resistant prostate cancer. *Siberian Journal of Oncology.* 2021;20(3):115–123. EDN: DIJSIE doi: 10.21294/1814-4861-2021-20-3-115-123

7. Pezaro CJ, Omlin A, Lorente D, et al. Visceral Disease in Castration-resistant Prostate Cancer. *Eur Urol.* 2014;65(2):270–273. doi: 10.1016/j.eururo.2013.10.055

8. Clezardin P, Coleman R, Puppo M, et al. Bone metastasis: mechanisms, therapies, and biomarkers. *Physiol Rev.* 2021;101(3):797–855. doi: 10.1152/physrev.00012.2019

9. Zhang X. Interactions between cancer cells and bone microenvironment promote bone metastasis in prostate cancer. *Cancer Commun.* 2019;39(1):76. doi: 10.1186/s40880-019-0425-1
10. Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. *Lancet.* 2020;395(10231):1208–1216. doi: 10.1016/S0140-6736(20)30314-7
11. Awenat S, Piccardo A, Carvoeiras P, et al. Diagnostic Role of 18F-PSMA-1007 PET/CT in Prostate Cancer Staging: A Systematic Review. *Diagnostics.* 2021:11(3):552. doi: 10.3390/diagnostics11030552
12. Alberts I, Sachpekidis C, Fech V, et al. PSMA-negative prostate cancer and the continued value of choline-PET/CT. *Nuklearmedizin.* 2020;59(1):33–34. doi: 10.1055/a-1044-1855
13. Sartor O, Baghian A. Prostate specific membrane antigen binding radiopharmaceuticals: Current data and new concepts. *Front Med (Lausanne).* 2022;9(1060922). doi: 10.3389/fmed.2022.1060922
14. Plichta KA, Graves SA, Buatti JM. Prostate-Specific Membrane Antigen (PSMA) Theranostics for Treatment of Oligometastatic Prostate Cancer. *Int J Mol Sci.* 2021;22(22):12095. doi: 10.3390/ijms222212095
15. Sun M, Niaz MJ, Niaz MO, et al. Prostate-Specific Membrane Antigen (PSMA)-Targeted Radionuclide Therapies for Prostate Cancer. *Curr Oncol Rep.* 2021; 23(5):59. doi: 10.1007/s11912-021-01042-w
16. Alberts I, Sachpekidis C, Dijkstra L, et al. The role of additional late PSMA-ligand PET/CT in the differentiation between lymph node metastases and ganglia. *Eur J Nucl Med Mol Imaging.* 2020;47(3):642–651. doi: 10.1007/s00259-019-04552-9
17. Khreish F, Ebert N, Ries M, et al. ^{225}Ac-PSMA-617/^{177}Lu-PSMA-617 tandem therapy of metastatic castration-resistant prostate cancer: pilot experience. *Eur J Nucl Med Mol Imaging.* 2020;47(3):721–728. doi: 10.1007/s00259-019-04612-0
18. Kendrick J, Francis R, Hassan GM, et al. Radiomics for Identification and Prediction in Metastatic Prostate Cancer: A Review of Studies. *Front Oncol.* 2021;11:771–787. doi: 10.3389/fonc.2021.771787
19. Macedo F, Ladeira K, Pinho F, et al. Bone metastases: an overview. *Oncol Rev.* 2017;11(1):321. doi: 10.4081/oncol.2017.321
20. Kitagawa Y, Yamaoka T, Yokouchi M, et al. Diagnostic Value of Plain Radiography for Symptomatic Bone Metastasis at the First Visit. *J Nippon Med Sch.* 2018;85(6):315–321. doi: 10.1272/jnms.JNMS.2018_85-51
21. Cornford P, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II–2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer. *Eur Urol.* 2021;79(2):263–282. doi: 10.1016/j.eururo.2020.09.046
22. Liu T, Wang S, Liu H, et al. Detection of vertebral metastases: a meta-analysis comparing MRI, CT, PET, BS and BS with SPECT. *J Cancer Res Clin Oncol.* 2017;143(3):457–465. doi: 10.1007/s00432-016-2288-z
23. Sergeev NI, Kotlyarov PM, Teplyakov VV, et al. Features of the application of diagnostic imaging methods in evaluating the results of treatment of bone metastases. *Russian Electronic Journal of Radiology.* 2021;11(4):84–93. EDN: YQNNKI doi: 10.21294/1814-4861-2018-17-1-5-10
24. Chen Z, Chen X, Wang R. Application of SPECT and PET / CT with computer-aided diagnosis in bone metastasis of prostate cancer: a review. *Cancer Imaging.* 2022;22(1):18. doi: 10.1186/s40644-022-00456-4
25. Steinhauer V, Sergeev NI. Radiomics in Breast Cancer: In-Depth Machine Analysis of MR Images of Metastatic Spine Lesion. *Sovremennye tehnologii v medicine.* 2022;14(2):16. doi: 10.17691/stm2022.14.2.02
26. Vilanova JC, Garcia-Figueiras R, Luna A, et al. Update on Whole-body MRI in Musculoskeletal Applications. *Semin Musculoskelet Radiol.* 2019;23(3):312–323. doi: 10.1055/s-0039-1685540
27. Padhani AR, Lecouvet FE, Tunariu N, et al. Rationale for Modernising Imaging in Advanced Prostate Cancer. *Eur Urol Focus.* 2017:3(2–3):223–239. doi: 10.1016/j.euf.2016.06.018
28. Karman AV, Abakumova EA, Shimanets SV, et al. Multiparametric MRI prostate cancer detection and staging. *Oncological journal.* 2019;1(49):136–147. EDN: VTNFYB
29. Perez-Lopez R, Mateo J, Mossop H, et al. Diffusion-weighted Imaging as a Treatment Response Biomarker for Evaluating Bone Metastases in Prostate Cancer: A Pilot Study. *Radiology.* 2017;283(1):168–177. doi: 10.1148/radiol.2016160646
30. Nakanishi K, Tanaka J, Nakaya Y, et al. Whole-body MRI: detecting bone metastases from prostate cancer. *Jpn J Radiol.* 2022;40(3):229–244. doi: 10.1007/s11604-021-01205-6
31. Sun G, Zhang Y.X., Liu F., et al. Whole-body magnetic resonance imaging is superior to skeletal scintigraphy for the detection of bone metastatic tumors: a meta-analysis. *Eur Rev Med Pharmacol Sci.* 2020;24(13):7240–7252. doi: 10.26355/eurrev_202007_21879
32. Padhani AR, Lecouvet FE, Tunariu N, et al. METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer. *Eur Urol.* 2017;71(1):81–92. doi: 10.1016/j.eururo.2016.05.033
33. Van den Wyngaert T, Strobel K, Kampen WU, et al. The EANM practice guidelines for bone scintigraphy. *Eur J Nucl Med Mol Imaging.* 2016;43(9):1723–1738. doi: 10.1007/s00259-016-3415-4
34. Scher HI, Morris MJ, Stadler WM, et al. Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. *J Clin Oncol.* 2016;34(12):1402–1418. doi: 10.1200/JCO.2015.64.2702
35. Anand A, Heller G, Fox J, et al. Automated Bone Scan Index to Optimize Prostate Cancer Working Group Radiographic Progression Criteria for Men With Metastatic Castration-Resistant Prostate Cancer. *Clin Genitourin Cancer.* 2022;20(3):270–277. doi: 10.1016/j.clgc.2022.02.002
36. Chao HS, Chang CP, Chiu CH, et al. Bone Scan Flare Phenomenon in Non-Small-Cell Lung Cancer Patients Treated With Gefitinib. *Clin Nucl Med.* 2009;34(6):346–349. doi: 10.1097/RLU.0b013e3181a344df
37. van der Zande K, Oyen WJG, Zwart W, et al. Radium-223 Treatment of Patients with Metastatic Castration Resistant Prostate Cancer: Biomarkers for Stratification and Response Evaluation. *Cancers (Basel).* 2021;13(17):4346. doi: 10.3390/cancers13174346
38. Nakajima K, Edenbrandt L, Mizokami A. Bone scan index: A new biomarker of bone metastasis in patients with prostate cancer. *Int J Urol.* 2017;24(9):668–673. doi: 10.1111/iju.13386
39. Ruchalski K, Dewan R, Sai V, et al. Imaging response assessment for oncology: An algorithmic approach. *Eur J Radiol Open.* 2022;9:100426. doi: 10.1016/j.ejro.2022.100426
40. Eremenko AV, Kosyh NE, Razuvaev VA, et al. Investigation of computer automated analysis capabilities for the effective diagnosis of disseminated prostate cancer. *Diagnostic radiology and radiotherapy.* 2019;1:74–85. EDN: NQOKHZ doi: 10.22328/2079-5343-2019-10-1-74-85
41. Dennis ER, Jia X, Mezheritskiy IS, et al. Bone Scan Index: A Quantitative Treatment Response Biomarker for Castration-Resistant Metastatic Prostate Cancer. *J Clin Oncol.* 2012;30(5):519–524. doi: 10.1200/JCO.2011.36.5791

42. Sheikhbahaei S., Jones K.M., Werner R.A., et al. ^{18}F-NaF-PET/CT for the detection of bone metastasis in prostate cancer: a meta-analysis of diagnostic accuracy studies. *Ann Nucl Med.* 2019;33(5): 351–361. doi: 10.1007/s12149-019-01343-y
43. Shen G, Deng H, Hu S, et al. Comparison of choline-PET/CT, MRI, SPECT, and bone scintigraphy in the diagnosis of bone metastases in patients with prostate cancer: a meta-analysis. *Skeletal Radiol.* 2014;43(11):1503–1513. doi: 10.1007/s00256-014-1903-9
44. Sergeev NI, Fomin DK, Kotlyarov PM, et al. Comparative Study of the Possibilities of Bone Scintigraphy and Magnetic Resonance Imaging of the Whole Body in the Diagnosis of Bone Metastases. *Medical Visualization.* 2014;4:107–113. EDN: SNIDQB
45. Blackwell W. Radiology-Nuclear Medicine Diagnostic Imaging: A Correlative Approach. First. Edited by Gholamrezanezhad A, Assadi M, Jadvar H USA. 2023.
46. Mohd Rohani MF, Mat Nawi N, Shamim SE, et al. Maximum standardized uptake value from quantitative bone single-photon emission computed tomography/computed tomography in differentiating metastatic and degenerative joint disease of the spine in prostate cancer patients. *Ann Nucl Med.* 2020;34(1):39–48. doi: 10.1007/s12149-019-01410-4
47. Okamoto S, Thieme A, Allmann J, et al. Radiation Dosimetry for 177Lu-PSMA I&T in Metastatic Castration-Resistant Prostate Cancer: Absorbed Dose in Normal Organs and Tumor Lesions. *J Nucl Med.* 2017;58(3):445–450. doi: 10.2967/jnumed.116.178483
48. Ghodsirad MA, Pirayesh E, Akbarian R, et al. Diagnostic Utility of Lutetium-177 (Lu 177) Prostate-Specific Membrane Antigen (PSMA) Scintigraphy In Prostate Cancer Patients With PSA Rise And Negative Conventional Imaging. *Urol J.* 2020; 23;17(4):374–378. doi: 10.22037/uj.v0i0.5451
49. Venkatachalapathy VSS, Rajeshkannan R, Sarma M, et al. Comparison of whole-body bone scintigraphy with axial skeleton magnetic resonance imaging in the skeletal evaluation of carcinoma prostate. *Indian J Urol.* 2021;37(1):72–78. doi: 10.4103/iju.IJU_238_20
50. Sergeev NI, Fomin DK, Kotlyarov PM, Solodkiy VA. Comparative study of the possibilities of SPECT/CT and whole body MRI in the diagnosis of bone metastases. *Bulletin of the Russian Scientific Center of Roentgenoradiology.* 2015;15(3):8. EDN: UXMAVX
51. Li R, Ravizzini GC, Gorin MA, et al. The use of PET/CT in prostate cancer. *Prostate Cancer Prostatic Dis.* 2018;21(1):4–21. doi: 10.1038/s41391-017-0007-8
52. Azad GK, Cook GJ. Multi-technique imaging of bone metastases: spotlight on PET-CT. *Clin Radiol.* 2016;71(7):620–631. doi: 10.1016/j.crad.2016.01.026
53. Kannivelu A, Loke K, Kok T, et al. The Role of PET/CT in the Evaluation of Skeletal Metastases. *Semin Musculoskelet Radiol.* 2014;18(2):149–165. doi: 10.1055/s-0034-1371017
54. Jadvar H. Molecular Imaging of Prostate Cancer: PET Radiotracers. *AJR Am J Roentgenol.* 2012;199(2):278–291. doi: 10.2214/AJR.12.8816
55. Alam MR, Singh SB, Thapaliya S, et al. A Review of ^{177}Lutetium-PSMA and ^{225}Actinium-PSMA as Emerging Theranostic Agents in Prostate Cancer. *Cureus.* 2022; 14(9):29369. doi: 10.7759/cureus.29369
56. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45(2):228–247. doi: 10.1016/j.ejca.2008.10.026
57. Acar E, Özdoğan Ö, Aksu A, et al. The use of molecular volumetric parameters for the evaluation of Lu-177 PSMA I&T therapy response and survival. *Ann Nucl Med.* 2019;33(9):681–688. doi: 10.1007/s12149-019-01376-3
58. Maffey-Steffan J, Scarpa L, Svirydenka A, et al. The ^{68}Ga/^{177}Lu-theragnostic concept in PSMA-targeting of metastatic castration-resistant prostate cancer: impact of post-therapeutic whole-body scintigraphy in the follow-up. *Eur J Nucl Med Mol Imaging.* 2020;47(3):695–712. doi: 10.1007/s00259-019-04583-2
59. O J, Lodge M, Wahl R. Practical PERCIST: A Simplified Guide to PET Response Criteria in Solid Tumors 1.0. *Radiology.* 2016;280(2):576–584. doi: 10.1148/radiol.2016142043
60. Schmuck S, von Klot CA, Henkenberens C, et al. Initial Experience with Volumetric 68 Ga-PSMA I&T PET/CT for Assessment of Whole-Body Tumor Burden as a Quantitative Imaging Biomarker in Patients with Prostate Cancer. *J Nucl Med.* 2017;58(12):1962–1968. doi: 10.2967/jnumed.117.193581
61. Tanaka K, Norikane T, Mitamura K, et al. Quantitative [^{99m}Tc]Tc-MDP SPECT/CT correlated with [18F]NaF PET/CT for bone metastases in patients with prostate cancer. *EJNMMI Phys.* 2022;9(1):83. doi: 10.1186/s40658-022-00513-8
62. Vlachostergios PJ, Niaz MJ, Sun M, et al. Prostate-Specific Membrane Antigen Uptake and Survival in Metastatic Castration-Resistant Prostate Cancer. *Front Oncol.* 2021;11:630589. doi: 10.3389/fonc.2021.630589
63. Beyersdorff D, Rahbar K, Essler M, et al. Interdisziplinärer Expertenkonsensus zu Innovationen der bildgebenden Diagnostik und radionuklidbasierten Therapien des fortgeschrittenen Prostatakarzinoms. *Urologe A.* 2021;60:1579–1585. doi: 10.1007/s00120-021-01598-2
64. Gafit A, Rauscher I, Weber M, et al. Novel Framework for Treatment Response Evaluation Using PSMA PET/CT in Patients with Metastatic Castration-Resistant Prostate Cancer (RECIP 1.0): An International Multicenter Study. *J Nucl Med.* 2022;63(11):1651–1658. doi: 10.2967/jnumed.121.263072
65. Isaac A, Dalili D, Dalili D, et al. State-of-the-art imaging for diagnosis of metastatic bone disease. *Radiologe.* 2020;60(1):1–16. doi: 10.1007/s00117-020-00666-6

СПИСОК ЛИТЕРАТУРЫ

1. Каприн А.Д., Алексеев Б.Я., Матвеев В.Б., и др. Рак предстательной железы. Клинические рекомендации // Общероссийский национальный союз «Ассоциация онкологов России». 2021. https://oncology-association.ru/wp-content/uploads/2021/02/rpzh.pdf. Дата обращения: 24.03.2024. EDN: RLCXWE
2. Gevorkyan A.R., Molodtsov M.S., Aleksandrov E.V. Prostate cancer diagnosis as part of high-tech advanced outpatient medical care // Urology Herald. 2023. Vol. 11, N 1. P. 26–33. doi: 10.21886/2308-6424-2023-11-1-26-33
3. Ling S.W., de Blois E., Hooijman E., et al. Advances in ^{177}Lu-PSMA and ^{225}Ac-PSMA Radionuclide Therapy for Metastatic Castration-Resistant Prostate Cancer // Pharmaceutics. 2022. Vol. 14, N 10. P. 2166. doi: 10.3390/pharmaceutics14102166
4. Sekhoacha M., Riet K., Motloung P., et al. Prostate Cancer Review: Genetics, Diagnosis, Treatment Options, and Alternative Approaches // Molecules. 2022. Vol. 27, N 17. P. 5730. doi: 10.3390/molecules27175730

5. Солодкий В.А., Павлов А.Ю., Фомин Д.К., и др. Определение роли Лютеция-ПСМА и других препаратов, нацеленных на ПСМА, при раке предстательной железы // Вестник РНЦРР. 2022. Т. 22, № 2. С. 27–36. EDN: UNNDSN

6. Медведева А.А., Чернов В.И., Усынин Е.А., и др. Использование ^{177}Lu-ПСМА для радионуклидной терапии у пациентов с кастрационно-резистентным раком предстательной железы // Сибирский онкологический журнал. 2021. Т. 20, № 3. С. 115–123. EDN: DIJSIE doi: 10.21294/1814-4861-2021-20-3-115-123

7. Pezaro C., Omlin A., Lorente D., et al. Visceral Disease in Castration-resistant Prostate Cancer // Eur Urol. 2014. Vol. 65, N 2. P. 270–273. doi: 10.1016/j.eururo.2013.10.055

8. Clezardin P., Coleman R., Puppo M., et al. Bone metastasis: mechanisms, therapies, and biomarkers // Physiol Rev. 2021. Vol. 101, N 3. P. 797–855. doi: 10.1152/physrev.00012.2019

9. Zhang X. Interactions between cancer cells and bone microenvironment promote bone metastasis in prostate cancer // Cancer Commun. 2019. Vol. 39, N 1. P. 76. doi: 10.1186/s40880-019-0425-1

10. Hofman M., Lawrentschuk N., Francis R., et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study // Lancet. 2020. Vol. 395, N 10231. P. 1208–1216. doi: 10.1016/S0140-6736(20)30314-7

11. Awenat S., Piccardo A., Carvoeiras P., et al. Diagnostic Role of ^{18}F-PSMA-1007 PET/CT in Prostate Cancer Staging: A Systematic Review // Diagnostics. 2021. Vol. 11, N 3. P. 552. doi: 10.3390/diagnostics11030552

12. Alberts I., Sachpekidis C., Fech V., et al. PSMA-negative prostate cancer and the continued value of choline-PET/CT // Nuklearmedizin. 2020. Vol. 59, N 1. P. 33–34. doi: 10.1055/a-1044-1855

13. Sartor O., Baghian A. Prostate specific membrane antigen binding radiopharmaceuticals: Current data and new concepts // Front Med (Lausanne). 2022. Vol. 9, 1060922. doi: 10.3389/fmed.2022.1060922

14. Plichta K., Graves S., Buatti J. Prostate-Specific Membrane Antigen (PSMA) Theranostics for Treatment of Oligometastatic Prostate Cancer // Int J Mol Sci. 2021. Vol. 22, N 22. P. 12095. doi: 10.3390/ijms222212095

15. Sun M., Niaz M., Niaz M., et al. Prostate-Specific Membrane Antigen (PSMA)-Targeted Radionuclide Therapies for Prostate Cancer // Curr Oncol Rep. 2021. Vol. 23, N 5. P. 59. doi: 10.1007/s11912-021-01042-w

16. Alberts I., Sachpekidis C., Dijkstra L., et al. The role of additional late PSMA-ligand PET/CT in the differentiation between lymph node metastases and ganglia // Eur J Nucl Med Mol Imaging. 2020. Vol. 47, N 3. P. 642–651. doi: 10.1007/s00259-019-04552-9

17. Khreish F., Ebert N., Ries M., et al. ^{225}Ac-PSMA-617/^{177}Lu-PSMA-617 tandem therapy of metastatic castration-resistant prostate cancer: pilot experience // Eur J Nucl Med Mol Imaging. 2020. Vol. 47, N 3. P. 721–728. doi: 10.1007/s00259-019-04612-0

18. Kendrick J., Francis R., Hassan G.M., et al. Radiomics for Identification and Prediction in Metastatic Prostate Cancer: A Review of Studies // Front Oncol. 2021. Vol. 11, P. 771–787. doi: 10.3389/fonc.2021.771787

19. Macedo F., Ladeira K., Pinho F., et al. Bone metastases: an overview // Oncol Rev. 2017. Vol. 11, N 1. P. 321. doi: 10.4081/oncol.2017.321

20. Kitagawa Y., Yamaoka T., Yokouchi M., et al. Diagnostic Value of Plain Radiography for Symptomatic Bone Metastasis at the First Visit // J Nippon Med Sch. 2018. Vol. 85, N 6. P. 315–321. doi: 10.1272/jnms.JNMS.2018_85-51

21. Cornford P., van den Bergh R.C.N., Briers E., et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II–2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer // Eur Urol. 2021. Vol. 79, N 2. P. 263–282. doi: 10.1016/j.eururo.2020.09.046

22. Liu T., Wang S., Liu H., et al. Detection of vertebral metastases: a meta-analysis comparing MRI, CT, PET, BS and BS with SPECT // J Cancer Res Clin Oncol. 2017. Vol. 143, N 3. P. 457–465. doi: 10.1007/s00432-016-2288-z

23. Сергеев Н.И., Котляров П.М., Солодкий В.А. Стандарты анализа метастатического поражения костных структур по данным современных методов лучевой диагностики // Сибирский онкологический журнал. 2018. Т. 17. № 1. С. 5–10. EDN: YQNNKI doi: 10.21294/1814-4861-2018-17-1-5-10

24. Chen Z., Chen X., Wang R. Application of SPECT and PET / CT with computer-aided diagnosis in bone metastasis of prostate cancer: a review // Cancer Imaging. 2022. Vol. 22, N 1. P. 18. doi: 10.1186/s40644-022-00456-4

25. Steinhauer V., Sergeev N.I. Radiomics in Breast Cancer: In-Depth Machine Analysis of MR Images of Metastatic Spine Lesion // Sovrem Tekhnologii Med. 2022. Vol. 14, N 2. P. 16–24. doi: 10.17691/stm2022.14.2.02

26. Vilanova J., Garcia-Figueiras R., Luna A., et al. Update on Whole-body MRI in Musculoskeletal Applications // Semin Musculoskelet Radiol. 2019. Vol. 23, N 3. P. 312–323. doi: 10.1055/s-0039-1685540

27. Padhani A.R., Lecouvet F.E., Tunariu N., et al. Rationale for Modernising Imaging in Advanced Prostate Cancer // Eur Urol Focus. 2017. Vol. 3, N 2–3. P. 223–239. doi: 10.1016/j.euf.2016.06.018

28. Карман А.В. Абакумова Е.А., Шиманец С.В., и др. Мультипараметрическая МРТ в диагностике и стадировании рака предстательной железы // Онкологический журнал. 2019. Т. 1, № 49. С. 136–147. EDN: VTNFYB

29. Perez-Lopez R., Mateo J., Mossop H., et al. Diffusion-weighted Imaging as a Treatment Response Biomarker for Evaluating Bone Metastases in Prostate Cancer: A Pilot Study // Radiology. 2017. Vol. 283, N 1. P. 168–177. doi: 10.1148/radiol.2016160646

30. Nakanishi K., Tanaka J., Nakaya Y., et al. Whole-body MRI: detecting bone metastases from prostate cancer // Jpn J Radiol. 2022. Vol. 40, N 3. P. 229–244. doi: 10.1007/s11604-021-01205-6

31. Sun G., Zhang Y., Liu F., et al. Whole-body magnetic resonance imaging is superior to skeletal scintigraphy for the detection of bone metastatic tumors: a meta-analysis // Eur Rev Med Pharmacol Sci. 2020. Vol. 24, N 13. P. 7240–7252. doi: 10.26355/eurrev_202007_21879

32. Padhani A., Lecouvet F., Tunariu N., et al. METastasis Reporting and Data System for Prostate Cancer: Practical Guidelines for Acquisition, Interpretation, and Reporting of Whole-body Magnetic Resonance Imaging-based Evaluations of Multiorgan Involvement in Advanced Prostate Cancer // Eur Urol. 2017. Vol. 71, N 1. P. 81–92. doi: 10.1016/j.eururo.2016.05.033

33. Van den Wyngaert T., Strobel K., Kampen W., et al. The EANM practice guidelines for bone scintigraphy // Eur J Nucl Med Mol Imaging. 2016. Vol. 43, N 9. P. 1723–1738. doi: 10.1007/s00259-016-3415-4

34. Scher H., Morris M., Stadler W., et al. Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3 // J Clin Oncol. 2016. Vol. 34, N 12. P. 1402–1418. doi: 10.1200/JCO.2015.64.2702

35. Anand A., Heller G., Fox J., et al. Automated Bone Scan Index to Optimize Prostate Cancer Working Group Radiographic Progression Criteria for Men With Metastatic Castration-Resistant Prostate Cancer // Clin Genitourin Cancer. 2022. Vol. 20, N 3. P. 270–277. doi: 10.1016/j.clgc.2022.02.002

36. Chao H., Chang C., Chiu C., et al. Bone Scan Flare Phenomenon in Non–Small–Cell Lung Cancer Patients Treated With Gefitinib // Clin Nucl Med. 2009. Vol. 34, N 6. P. 346–349. doi: 10.1097/RLU.0b013e3181a344df
37. van der Zande K., Oyen W.J.G., Zwart W., et al. Radium-223 Treatment of Patients with Metastatic Castration Resistant Prostate Cancer: Biomarkers for Stratification and Response Evaluation // Cancers (Basel). 2021. Vol. 13, N 17. P. 4346. doi: 10.3390/cancers13174346
38. Nakajima K., Edenbrandt L., Mizokami A. Bone scan index: A new biomarker of bone metastasis in patients with prostate cancer // Int J Urol. 2017. Vol. 24, N 9. P. 668–673. doi: 10.1111/iju.13386
39. Ruchalski K., Dewan R., Sai V., et al. Imaging response assessment for oncology: An algorithmic approach // Eur J Radiol Open. 2022. Vol. 9, P. 100426. doi: 10.1016/j.ejro.2022.100426
40. Еременко А.В., Косых Н.Э., Разуваев В.А., Савин С.З. Исследование возможностей компьютерного автоматизированного анализа для задач эффективной диагностики диссеминированного рака предстательной железы // Лучевая диагностика и терапия. 2019. № 1. С. 74–85. EDN: NQOKHZ doi: 10.22328/2079-5343-2019-10-1-74-85
41. Dennis E., Jia X., Mezheritskiy I., et al. Bone Scan Index: A Quantitative Treatment Response Biomarker for Castration-Resistant Metastatic Prostate Cancer // J Clin Oncol. 2012. Vol. 30, N 5. P. 519–524. doi: 10.1200/JCO.2011.36.5791
42. Sheikhbahaei S., Jones K., Werner R., et al. ^{18}F-NaF-PET/CT for the detection of bone metastasis in prostate cancer: a meta-analysis of diagnostic accuracy studies // Ann Nucl Med. 2019 Vol. 33, N 5. P. 351–361. doi: 10.1007/s12149-019-01343-y
43. Shen G., Deng H., Hu S., et al. Comparison of choline-PET/CT, MRI, SPECT, and bone scintigraphy in the diagnosis of bone metastases in patients with prostate cancer: a meta-analysis // Skeletal Radiol. 2014. Vol. 43, N 11. P. 1503–1513. doi: 10.1007/s00256-014-1903-9
44. Сергеев Н.И., Фомин Д.К., Котляров П.М., и др. Сравнительное исследование возможностей остеосцинтиграфии и магнитно-резонансной томографии всего тела в диагностике костных метастазов // Медицинская Визуализация. 2014. Т. 4. С. 107–113. EDN: SNIDQB
45. Blackwell W. Radiology-Nuclear Medicine Diagnostic Imaging: A Correlative Approach. First. ed. Gholamrezanezhad A., Assadi M., Jadvar H., editors. USA. 2023.
46. Mohd Rohani M., Mat Nawi N., Shamim S., et al. Maximum standardized uptake value from quantitative bone single-photon emission computed tomography/computed tomography in differentiating metastatic and degenerative joint disease of the spine in prostate cancer patients // Ann Nucl Med. 2020. Vol. 34, N 1. P. 39–48. doi: 10.1007/s12149-019-01410-4
47. Okamoto S., Thieme A., Allmann J., et al. Radiation Dosimetry for 177Lu-PSMA I&T in Metastatic Castration-Resistant Prostate Cancer: Absorbed Dose in Normal Organs and Tumor Lesions // J Nucl Med. 2017. Vol. 58, N 3. P. 445–450. doi: 10.2967/jnumed.116.178483
48. Ghodsirad M., Pirayesh E., Akbarian R., et al. Diagnostic Utility of Lutetium-177 (Lu 177) Prostate-Specific Membrane Antigen (PSMA) Scintigraphy In Prostate Cancer Patients With PSA Rise And Negative Conventional Imaging // Urol J. 2020. Vol. 17, N 4. P. 374–378. doi: 10.22037/uj.v0i0.5451
49. Venkatachalapathy V., Rajeshkannan R., Sarma M., et al. Comparison of whole-body bone scintigraphy with axial skeleton magnetic resonance imaging in the skeletal evaluation of carcinoma prostate // Indian J Urol. 2021. Vol. 37, N 1. P. 72–78. doi: 10.4103/iju.IJU_238_20
50. Сергеев Н.И., Фомин Д.К., Котляров П.М., Солодкий В.А.. Сравнительное исследование возможностей ОФЭКТ/КТ и магнитно-резонансной томографии всего тела в диагностике костных метастазов // Вестник российского научного центра рентгенорадиологии. 2015. Т. 15, № 3. С. 8. EDN: UXMAVX
51. Li R., Ravizzini G., Gorin M., et al. The use of PET/CT in prostate cancer // Prostate Cancer Prostatic Dis. 2018. Vol. 21, N 1. P. 4–21. doi: 10.1038/s41391-017-0007-8
52. Azad G., Cook G. Multi-technique imaging of bone metastases: spotlight on PET-CT // Clin Radiol. 2016. Vol. 71, N 7. P. 620–631. doi: 10.1016/j.crad.2016.01.026
53. Kannivelu A., Loke K., Kok T., et al. The Role of PET/CT in the Evaluation of Skeletal Metastases // Semin Musculoskelet Radiol. 2014. Vol. 18, N 2. P. 149–165. doi: 10.1055/s-0034-1371017
54. Jadvar H. Molecular Imaging of Prostate Cancer: PET Radiotracers // AJR Am J Roentgenol. 2012. Vol. 199, N 2. P. 278–291. doi: 10.2214/AJR.12.8816
55. Alam M., Singh S., Thapaliya S., et al. A Review of ^{177}Lutetium-PSMA and ^{225}Actinium-PSMA as Emerging Theranostic Agents in Prostate Cancer // Cureus. 2022. Vol. 14, N 9. P. 29369. doi: 10.7759/cureus.29369
56. Eisenhauer E., Therasse P., Bogaerts J., et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1) // Eur J Cancer. 2009. Vol. 45, N 2. P. 228–247. doi: 10.1016/j.ejca.2008.10.026
57. Acar E., Özdoğan Ö., Aksu A., et al. The use of molecular volumetric parameters for the evaluation of Lu-177 PSMA I&T therapy response and survival // Ann Nucl Med. 2019. Vol. 33, N 9. P. 681–688. doi: 10.1007/s12149-019-01376-3
58. Maffey-Steffan J., Scarpa L., Svirydenka A., et al. The ^{68}Ga/^{177}Lu-theragnostic concept in PSMA-targeting of metastatic castration-resistant prostate cancer: impact of post-therapeutic whole-body scintigraphy in the follow-up // Eur J Nucl Med Mol Imaging. 2020. Vol. 47, N 3. P. 695–712. doi: 10.1007/s00259-019-04583-2
59. O J., Lodge M., Wahl R. Practical PERCIST: A Simplified Guide to PET Response Criteria in Solid Tumors 1.0 // Radiology. 2016. Vol. 280, N 2. P. 576–584. doi: 10.1148/radiol.2016142043
60. Schmuck S., von Klot C., Henkenberens C., et al. Initial Experience with Volumetric 68 Ga-PSMA I&T PET/CT for Assessment of Whole-Body Tumor Burden as a Quantitative Imaging Biomarker in Patients with Prostate Cancer // Journal of Nuclear Medicine. 2017. Vol. 58, N 12. P. 1962–1968. doi: 10.2967/jnumed.117.193581
61. Tanaka K., Norikane T., Mitamura K., et al. Quantitative [^{99m}Tc] Tc-MDP SPECT/CT correlated with [18F]NaF PET/CT for bone metastases in patients with prostate cancer // EJNMMI Phys. 2022. Vol. 9, N 1. P. 83. doi: 10.1186/s40658-022-00513-8
62. Vlachostergios P., Niaz M., Sun M., et al. Prostate-Specific Membrane Antigen Uptake and Survival in Metastatic Castration-Resistant Prostate Cancer // Front Oncol. 2021. Vol. 11, P. 630589. doi: 10.3389/fonc.2021.630589
63. Beyersdorff D., Rahbar K., Essler M., et al. Interdisziplinärer Expertenkonsensus zu Innovationen der bildgebenden Diagnostik und radionuklidbasierten Therapien des fortgeschrittenen Prostatakarzinoms // Urologe. 2021. Vol. 60, P. 1579–1585. doi: 10.1007/s00120-021-01598-2
64. Gafita A., Rauscher I., Weber M., et al. Novel Framework for Treatment Response Evaluation Using PSMA PET/CT in Patients with Metastatic Castration-Resistant Prostate Cancer (RECIP 1.0): An International Multicenter Study // J Nucl Med. 2022. Vol. 63, N 11. P. 1651–1658. doi: 10.2967/jnumed.121.263072
65. Isaac A., Dalili D., Dalili D., Weber M. State-of-the-art imaging for diagnosis of metastatic bone disease // Radiologe. 2020. Vol. 60, N 1. P. 1–16. doi: 10.1007/s00117-020-00666-6

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