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Объективные критерии МРТ-оценки эффективности лечения метастазов в кости у больных раком предстательной железы и раком молочной железы: систематический обзор и метаанализ

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АННОТАЦИЯ

Обоснование. Возможность персонализированного подхода к лечению метастатического рака предстательной железы (РПЖ) и рака молочной железы (РМЖ) требует объективных методов оценки ответа на лечение очагов в скелете. Доказанная высокая эффективность МРТ в выявлении метастазов в кости в сочетании с отсутствием ионизирующего излучения создаёт предпосылки для использования метода в мониторинге хода лечения на основе объективных критериев оценки терапевтического эффекта.

Цель — оценить возможности объективных количественных и полуколичественных МРТ-критериев в определении эффективности лечения (радио-, химио-, гормоно- и таргетная терапия) метастазов в кости, применявшихся в клинических исследованиях у больных РПЖ и РМЖ.

Материалы и методы. Поиск в базах данных Embase, PubMed, Cochrane Central Register of Controlled trials (CENTRAL), eLibrary осуществлялся до 01.06.2021 по ключевым словам «magnetic resonance imaging», «MRI», «DWI», «treatment response», «prostate cancer», «breast cancer», «bone metastasis» на английском и русском языках. В обзор включали только исследования по объективной МРТ-оценке эффективности любого типа лечебного воздействия (за исключением хирургии) при метастатическом поражении скелета.

Результаты. На основании анализа 11 исследований, отобранных из 312 источников, выделены 4 группы объективных МРТ-критериев оценки терапевтического эффекта при метастатическом поражении костей у больных РПЖ и РМЖ, включающих динамику размеров, интенсивности сигнала на диффузионно-взвешенном изображении, числовых значений измеряемого коэффициента диффузии (ИКД), общей опухолевой нагрузки. Изменения этих количественных и полуколичественных показателей во всех работах, за единственным исключением, имели одинаковую направленность, хотя и различались числовыми значениями. Учитывая статистически значимую гетерогенность ($p < 0,1$ для критерия χ^2 и при $I^2 > 40\%$) для значений ИКД до и после лечения, для анализа использовалась модель случайных эффектов. Изменение ИКД в результате лечения в среднем составило $+0,35 [+0,12; +0,49] \times 10^{-3} \text{ мм}^2/\text{с}$ со средними значениями ИКД до лечения $0,83 [0,71; 1,03] \times 10^{-3} \text{ мм}^2/\text{с}$, после лечения — $1,18 [0,83; 1,49] \times 10^{-3} \text{ мм}^2/\text{с}$.

Заключение. МРТ является информативной методикой для объективной оценки ответа костных метастазов на терапию у больных РПЖ и РМЖ на основе количественных и полуколичественных критериев и имеет значительный потенциал в качестве диагностического инструмента для мониторинга эффективности лечения метастатического поражения скелета.

Ключевые слова: магнитно-резонансная томография; метастазы в кости; ответ на лечение; метастатический рак молочной железы; метастатический рак предстательной железы.

Как цитировать

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Objective criteria for MRI evaluation of the effectiveness of treatment of bone metastases in patients with prostate cancer and breast cancer: systematic review and meta-analysis

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ABSTRACT

BACKGROUND: The possibility of a personalized approach to the treatment of metastatic prostate cancer and breast cancer requires objective methods for the evaluation of the response of foci treatment in the skeleton. The proven high efficiency of MRI in detecting bone metastases, in combination with the absence of ionizing radiation, has laid the groundwork for using this method in monitoring the treatment course based on objective criteria for evaluation of the therapeutic outcome.

AIM: To assess the possibilities of quantitative and semi-quantitative parameters of MRI-evaluation of treatment efficacy (radiation, chemotherapy, hormone therapy, and targeted therapy) of bone metastases that were used in prostate and breast cancer clinical trials.

MATERIALS AND METHODS: We searched the databases Embase, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), eLibrary until April 1, 2021, using the following keywords: magnetic resonance imaging, MRI, DWI, treatment response, prostate or breast cancer, and bone metastasis. We only included studies related to the MRI-evaluation of treatment efficacy of any type of therapeutic intervention (with the exception of surgery) for metastatic skeletal lesions in this review.

RESULTS: We selected and analyzed 11 out of 312 sources found as a result of the search. It allowed us to identify four groups of objective MRI criteria for evaluating the therapeutic effect in metastatic bone lesions in patients with prostate and breast cancer, including the dynamics of sizes, signal intensity on DWI, ADC, and tumor total diffusion volume (tDV). Changes in these quantitative and semi-quantitative indicators, with only one exception, had the same direction, although they differed in numerical values. A random-effects model was used for analysis considering the presence of statistically significant heterogeneity ($p < 0,1$ for χ^2 test; $I^2 > 40\%$). The change in ADC as a result of treatment averaged $+0.35 [+0.12; +0.49] \times 10^{-3} \text{ mm}^2/\text{s}$, with average values of ADC before treatment — $0.83 [0.71; 1.03] \times 10^{-3} \text{ mm}^2/\text{s}$, after treatment — $1.18 [0.83; 1.49] \times 10^{-3} \text{ mm}^2/\text{s}$.

CONCLUSION: MRI is an informative technique for the objective evaluation of the response of bone metastases to therapy in patients with prostate cancer and breast cancer based on quantitative and semi-quantitative parameters. It has significant potential as a diagnostic test instrument for monitoring the effectiveness of treatment of metastatic skeletal lesions.

Keywords: magnetic resonance imaging; bone metastasis; treatment response; metastatic breast cancer; metastatic prostate cancer.

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MRT评估前列腺癌和乳腺癌骨转移有效性的客观标准：系统评论和核心分析

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简评

论证转移性前列腺癌（PC）和乳腺癌（BC）的个体化治疗需要客观的方法来评估对骨骼病灶治疗的反应。经过验证的高效MRT在骨骼中鉴定与没有电离辐射的鉴定的组合产生的前提是使用该方法在监测基于评估治疗效果的客观标准治疗治疗方法时的先决条件。

目标是估计客观定量和半定量MRT标准的可能性，用于确定患有PC和BC患者的临床研究中使用的骨骼中的治疗的有效性（无线电，化学 - 激素和靶向治疗）。

材料与方Embase, PubMed数据库, Cochrane Central寄存器（中央），Elibrary通过关键词“磁共振成像”，“MRI”，“DWI”，“治疗反应”，“前列腺”癌症“，”乳腺癌“，英语和俄语”骨转移“。概述仅包括在骨架的转移病变期间对任何类型治疗效果（外科除外）有效性的客观MRT评估的研究。

结果。根据分析选自312次来源的11项研究，4组客观MRI标准，用于估算PC和BC患者骨骼的转移损伤期间的治疗效果，包括尺寸的动态；扩散加权图像上的信号强度；测量扩散系数（MDC）的数值；总肿瘤载荷。所有作品中，这些定量和半定量指标的变化在唯一的例外，虽然它们具有相同的焦点，但它们的数值不同。鉴于治疗前后的ICD值的统计学上显著的异质性（ $p < 0,1$ 对于 χ^2 标准和 $I^2 > 40\%$ ）进行治疗前后的MDC值，用于分析随机效应的模型。治疗导致的CDI变化平均为 $+0.35 [+0.12; +0.49] \times 10^{-3}$ 平方毫米/秒治疗前平均ADC值 $0.83 [0.71; 1.03] \times 10^{-3}$ 平方毫米/秒，处理后 $-1.18 [0.83; 1.49] \times 10^{-3}$ 平方毫米/秒。

结论MRI 是一种基于定量和半定量标准客观评估前列腺癌和乳腺癌患者骨转移对治疗反应的信息技术，具有作为监测转移性骨骼病变治疗效果的诊断工具的巨大潜力。

关键词：磁共振成像；骨转移；对治疗的反应；转移性乳腺癌；转移性前列腺癌。

引用本文

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Abbreviations

HT — hormone therapy	BC — breast cancer
DWI — diffusion-weighted imaging	PC — prostate cancer
ADC — apparent diffusion coefficient	RT — radiotherapy
SI — signal intensity	T1-WI — T1- weighted image
MRI — magnetic resonance imaging	TT — targeted therapy
PET-CT — positron emission tomography combined with computed tomography	CT — chemotherapy
	tDV — tumor total diffusion volume

INTRODUCTION

Metastatic skeletal lesions are common in disseminated prostate cancer (PC) and breast cancer (BC) and are found in 70%–80% of autopsies, sometimes the only localized distant metastases. In over 50% of patients, distant metastases begin with bone lesions [1–3].

Bone metastases lead to deterioration in the physical, functional, and emotional state of patients as well as a shortening in life expectancy. Although oligometastatic lesions can possibly be treated through radical therapy, the prognosis is much worse in disseminated lesions, with treatment becomes palliative (aimed at improving the overall quality of life of patients). Advancements in chemotherapy, hormone therapy and aggressive multimodal therapy allow for individualization and standardization on the assessment of the achieved therapeutic effect [4, 5].

Magnetic resonance imaging (MRI) is an effective method of detecting metastatic skeletal lesions with higher sensitivity and specificity rates (90.5% and 95%, respectively) compared with scintigraphy (72.9% and 93.9%), and comparable to combined choline positron emission tomography and computed tomography ([PET-CT] 89.7% and 96%) [6–8]. The MRI potential to assess the efficiency of bone metastasis treatment has been studied long enough by using the dynamics of the MR signal size and intensity on conventional images. The advent of diffusion-weighted imaging (DWI) and whole-body MRI has led to the generation of new criteria for assessing the response to the treatment of skeletal lesions. However, no unified approach has been developed for MRI assessment of the treatment efficiency of bone metastases based on objective criteria, and data on MRI findings of the responding lesions are contradictory [9–12].

The aim was to assess the possibilities of quantitative and semi-quantitative parameters of MRI-evaluation of treatment efficacy (radiation, chemotherapy, hormone therapy, and targeted therapy) of bone metastases that were used in PC and BC clinical trials.

METHODS

This paper is written according to the PRISMA criteria (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [13].

Eligibility criteria

Inclusion criteria: Eligible papers were selected according to the Population, Intervention, Comparison, Outcomes and Study principle [14]. Patients: 18 years of age or older with histologically confirmed BC or PC and metastatic bone lesions. Intervention: MRI of both individual areas and the whole body. The MRI protocol included standard anatomical pulse sequences (T1- and T2-weighted images and STIR) and/or DWI with apparent diffusion coefficient (ADC) mapping. Comparison group: None. Outcome: Bone metastases were scanned at least one week before and 1–6 months after the start of anticancer treatment; reference assessment of the treatment response was performed by comparing MRI data using laboratory diagnostic methods (blood prostate-specific antigen level), results of instrumental studies (spiral CT, skeletal scintigraphy, and PET-CT), and histological examination with assessment of therapeutic tumor pathomorphosis. Studies: Studies in which MRI was performed before and after 1–6 months from the start of anticancer treatment. No restrictions on the type of received therapy (chemical, hormonal, targeted, and radiotherapy) were used.

Non-inclusion criteria: Patients who received surgical treatment for metastatic bone lesions.

With regard to the technical MRI developments, the following studies were selected, including: DWI and ADC assessments that were published after January 1, 2010; and standard anatomic sequences that were published after January 1, 1998.

Exclusion criteria: Papers not written in Russian or English, conference abstracts, descriptions of clinical cases, and animal studies.

Sources of information

Publications were searched and selected from Embase, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and eLibrary electronic databases. Last search was on June 01, 2021.

Search: The search was conducted among prospective and retrospective clinical studies and randomized controlled studies using the following MeSH library terms and keywords: “Magnetic resonance imaging,” “DWI,” “treatment,” “response,” “prostate cancer,” “breast cancer,” and “bone metastasis.”

Study selection: The search and subsequent selection were conducted by two independent reviewers. Any discrepancies were resolved by the principal investigator. At the first stage, titles/proceedings/abstracts were reviewed for relevance to the review topic and the presence of necessary data. The second stage involved a full analysis of publications according to the inclusion and exclusion criteria.

Data collection: A tabular form was developed for data collection. Data was extracted by two reviewers including: title of the article, year of publication, authors, DOI, primary lesion, population, treatment, study duration, pulse sequences, reference method, MR semiotics, and ADC and signal intensity values before and after treatment.

Risk of bias: The QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) questionnaire was used to assess the risk of bias in individual studies [15]. The texts of articles were assessed according to the following criteria: patient enrollment, studied methods, reference methods, and time intervals between the study and reference methods. Certain questions from the QUADAS-2 checklist were not employed due to lack of necessity (for example, in the papers assessing the ADC, no question related to the study interpreter's blinding was used, since the ADC is an objective assessment). Finally, a histogram was generated after analyzing each study for the risk of bias.

Statistical analysis

The method for analyzing and grouping data (random-effects or fixed-effects model) was selected according to the results of heterogeneity assessment of studies that included ADC determination, which was performed using the χ^2 criterion and I^2 heterogeneity index. Heterogeneity of studies was considered significant at $p < 0.1$ for the χ^2 criterion and at $I^2 > 40\%$.

RESULTS

Study selection

The present study included 11 studies from 312 sources from Embase, PubMed, CENTRAL, and eLibrary databases (Fig. 1).

At the first stage, 273 sources were selected after sorting out duplicates (31) and animal studies (8). Next, 181 publications were sorted out after assessment of proceedings and abstracts at the screening stage. After checking full-text versions of the papers for inclusion criteria, 11 sources were remained and included in this review (Table).

We included 370 patients; among these, 147 patients responded to treatment. Three sources did not provide relevant information on the number of responders [5, 16, 17]. The sample size of each of the included studies ranged from 10 to 87 patients. Seven studies included only patients with a primary lesion in the prostate or mammary gland; four studies [5, 16, 20, 21] included these localizations in 85%–95% of the entire sample. The mean age of the patients was 47–73 years.

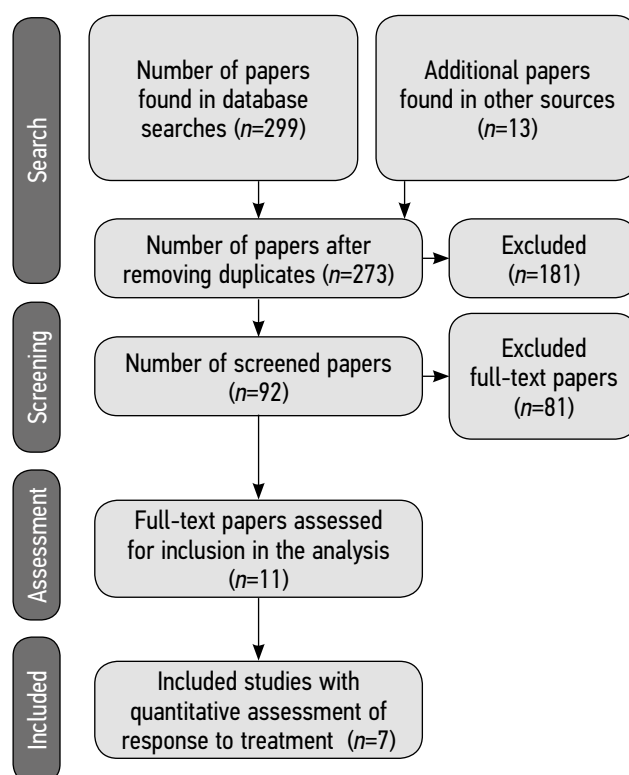


Fig. 1. PRISMA diagram of this study

The participants in the papers were divided into four groups according to the criteria which were used to assess the response to systemic therapy. These include size of metastatic lesions, DWI signal intensity, ADC, total tumor volume [5, 9–12, 16, 17, 20].

CT, skeletal scintigraphy, and prostate-specific antigen (in PC patients) were used as reference test [9–11, 16, 17, 20], whereas PET and biopsy were used in addition to these methods [5, 12]. Three papers did not contain data on the reference methods used [18, 19, 21].

Scanning parameters

The scanning parameters when using T1-SE-sequencing in different studies had slight differences in TR and TE values (400–600 ms and 5–16 ms, respectively). Only one paper had significantly different T1-WI parameters of 1000 ms and 3.7 ms. The number of b-factors was 2–3 with initial and highest values of 0–50 and 800–900, respectively [5, 10, 12, 13]. In one study [9], the number of b-factors was 4 (0, 50, 250, and 750), and in another study [20], it accounted for 6 (0, 50, 100, 250, 500, and 750), with obtaining higher ADC values compared with the other studies, which may result from changes in scanning parameters. The slice thickness in all studies was within 4–6 mm for both T1-WI and DWI images.

Classification of objective assessment criteria used in the literature

The first criterion for the therapeutic response of bone metastases was the change in the lesion size. Remarkably, bone lesions are recommended for measurements

Table. Characteristics of studies included in the systematic review and *meta-analysis*

No.	Authors	Year	Nosology	Treatment	Interval between studies	Magnetic field induction, T	MRI model and manufacturer	Objective criteria
1	Byun et al. [5]	2002	BC (90%)	RT	6 months	1.5	Not specified	ADC, SI (DWI)
2	Messiou et al. [9]	2011	PC	CT	3 months	1.5	Avanto, Siemens	ADC
3	Reischauer et al. [10]	2010	PC	HT	1–3 months	1.5	Achieva, Philips	ADC
4	Perez-Lopez et al. [11]	2016	PC	TT	3 months	1.5	Avanto, Siemens	ADC, tDV
5	Blackledge et al. [12]	2014	PC, BC	CT, HT, RT, TT	10–38 weeks	1.5	Avanto, Aera, Siemens	ADC, tDV
6	Sergeev et al. [16]	2016	BC, PC (90%)	CT, HT, RT	2–8 months	1.5	Excelart, Toshiba	ADC, SI (DWI)
7	Çiray et al. [17]	2001	BC	CT, HT	3–6 months	0.5	Gyroscan T5, Philips	Size
8	Brown et al. [18]	1998	BC	HT, CT, RT	6, 9 months	1.5	Vision, Siemens	Size
9	Tombal et al. [19]	2005	PC	CT	6 months	1.5	Intera, Philips	Size
10	Cappabianca et al. [20]	2014	PC, BC (90%)	RT	1, 2 months	1.5	Symphony, Siemens,	ADC, SI (DWI)
11	Kotlyarov et al. [21]	2006	BC, PC (75%)	CT, HT, RT	2–8 months	0.5	Proview Open, Philips	Size

Note. MRI, magnetic resonance imaging; BC, breast cancer; PC, prostate cancer; CT, chemotherapy; HT, hormone therapy; RT, radiotherapy; TT, targeted therapy; ADC, apparent diffusion coefficient; SI, signal intensity; DWI, diffusion-weighted images; tDV, tumor total diffusion volume.

on T1-WI due to higher contrast, clearer contours, and less pronounced perifocal edema [6, 22]. This criterion was used in 4 of 11 selected studies.

The second criterion for response assessment was semi-quantitative determination of DWI signal intensity, which was found in 3 of these papers. Since signal intensity is not a physical quantity, its numerical value may differ with different MRI scanners and at different scanning parameters. Therefore, the signal intensity ratio in metastases to the signal intensity in muscles was used.

The third criterion for assessing the response to treatment is the change in the numerical ADC value of the lesion. This criterion has been most widely used recently, including 7 of 11 selected papers; however, ADC values depend on imaging parameters.

The fourth and most novel criterion is the determination of the total diffusion volume (tDV), which is automatically calculated (in mL) using the maximum DWI intensity projection with a semi-automated and manually corrected 3D-mask by counting the number of voxels in a given range of signal intensities (Fig. 2). The distribution of the number of voxels over the ADC ranges, which correspond to responding, non-responding, and doubtful lesions, represented in a histogram [11, 12, 23].

Risk of bias

The risk of bias arises from differences in anticancer therapies and the time intervals between MRI before and after treatment. According to the QUADAS-2 criteria, the main point of the risk of bias was the selection of the

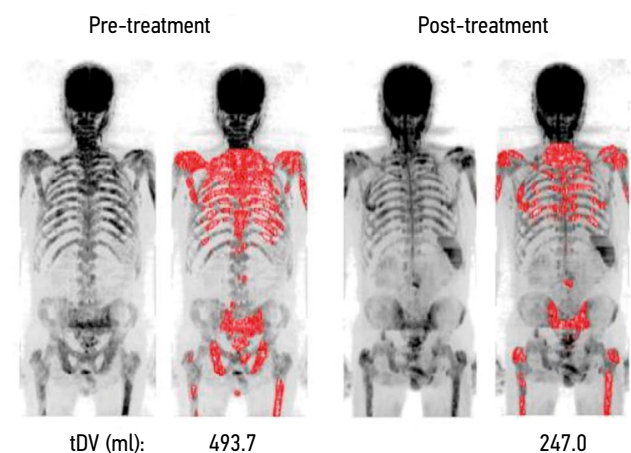


Fig. 2. Visualization and values of the total tumor volume before and after treatment in a patient with a significant response to systemic therapy

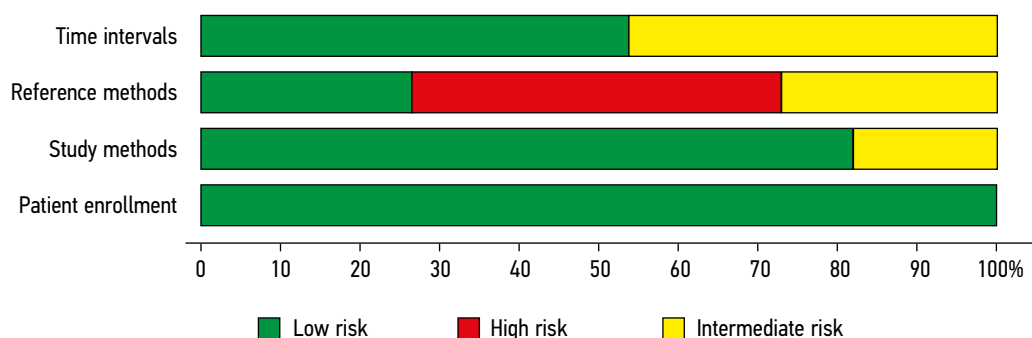


Fig. 3. Risk of bias according to QUADAS-2

reference methods (Fig. 3). Five papers used different imaging techniques for different patients as a reference [5, 12], or scintigraphy was used as a single method [16, 17, 20], which is inferior in diagnostic value to MRI and lacks the necessary values of sensitivity and specificity. The reference method was completely absent in three papers [18, 19, 21], and the assessment of the response to therapy was controlled by the level of prostate-specific antigen and clinical data. MR tomographs were used with a magnetic field intensity of 0.5 T, which might be an additional source of bias [17, 18].

Assessment results of bone lesion response to systemic therapy

Size: Changes in T1-WI size were assessed in four papers [17–19, 21]; among these, three showed a significant decrease in individual responding lesions and in tumor mass index, which was obtained as a result of sum of all metastatic lesion sizes in two dimensions. Moreover, B. Tombal et al. observed complete disappearance of metastatic lesions in two cases. However, the authors repeated the study after 6 months as opposed to a 2–3-month follow-up in other publications. On the contrary, Brown et al. reported constant sizes in 77% as opposed to an increased size in 23% of patients with responding lesions.

DWI signal intensity: Three studies contain data on DWI signal intensity changes in bone metastases as a result of systemic therapy [5, 16, 20]. In all studies, the authors came to the unequivocal conclusion that the signal intensity decreased significantly in response to treatment. However, only one presented numerical values that indicated a 35%

signal intensity reduction in lesions that responded to radiotherapy [20].

ADC: The assessment and analysis of quantitative ADC values were performed in seven papers [5, 9–12, 16, 20]. Sergeev et al. did not provide data for each patient or lesion; they demonstrated a 25% overall ADC increase in response to treatment of osteoblastic lesions and a 25% decrease in osteolytic lesions. Six papers presented accurate ADC values before and after treatment [5, 9–12, 20]. All authors noted increased ADC values in response to treatment of bone metastases, as reflected by the forest plot (Fig. 4) constructed using a random-effects model, given the presence of significant heterogeneity of the results ($p < 0.1$ for the χ^2 test and $I^2 > 40\%$).

The ADC changes after treatment averaged $+ 0.35 [+ 0.12; + 0.49] \times 10^{-3} \text{ mm}^2/\text{s}$. The range of baseline and post-therapy ADC values from all six papers is shown in Fig. 5 with mean ADC values before and after treatment, which accounted for $0.83 [0.71, 1.03]$ and $1.18 [0.83, 1.49] \times 10^{-3} \text{ mm}^2/\text{s}$, respectively. Despite partially overlapping values, the ADC was generally higher in responding patients as compared to values before treatment.

tDV: In two studies, tDV was assessed by DWI using special software [11, 12]. Mean tDV values in responding patients decreased by 59% according to Perez-Lopez et al. [11] and by 42.3% according to Blackledge et al. [12].

DISCUSSION

This systematic review demonstrates the assessment potential in the evaluation of the response to therapy of

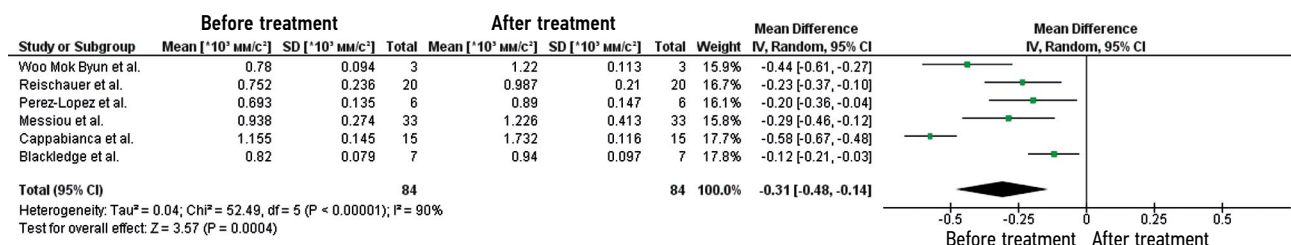


Fig. 4. Forest plot based on the results of studies that determined the changes in the apparent diffusion coefficient values in patients with bone metastases that responded to treatment

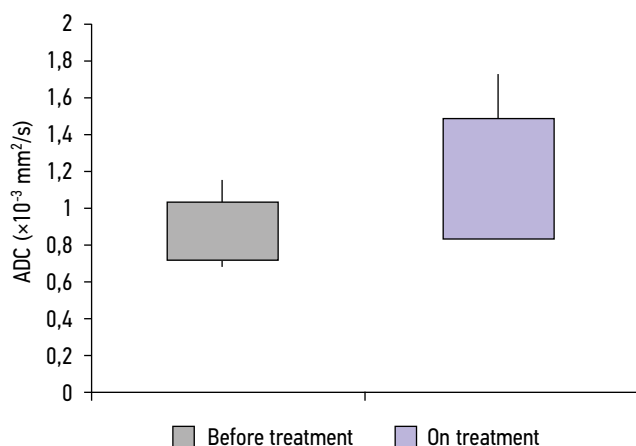


Fig. 5. Boxplot of the apparent diffusion coefficient values of bone metastases before treatment (gray) and after 1–6 months from the start of therapy (lilac), which was constructed according to the values of all included responding lesions ($n = 156$)

metastatic bone lesions based on the dynamics of objective criteria such as lesion size, relative DWI signal intensity, and ADC and tDV numerical values.

The relevance of this issue is due to the rapidly growing use of whole-body MRI for the primary diagnosis of bone metastases in patients with PC and BC [7, 8, 24, 25], who subsequently receive systemic therapy and radiotherapy and need to assess the treatment efficiency.

Assessment of the size of bone metastases as an objective indicator of the systemic therapy efficiency has long been used. RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) criteria are most commonly used for this purpose, according to which only osteolytic and mixed lesions with a soft tissue component of at least 10 mm are considered measurable bone lesions, whereas diffuse and osteoblastic lesions are considered unmeasurable [26, 27]. Despite existing limitations, the RECIST 1.1 criteria for bone lesions are included in the MET-RADSP (METastasis Reporting and Data System for Prostate Cancer) recommendations for whole-body MRI and are used along with the ADC to assess response in metastatic PC [1, 6].

The MDA criteria were developed specifically for the bone metastasis assessment at the University of Texas MD Anderson Cancer Center to assess any type of lesions based on the dynamics of their number, size, and structural features [27]. These criteria are applicable to both radiography and computed tomography, and MRI; however, they are less common compared with RECIST 1.1.

Assessment of the dynamics of bone metastasis size on T1-WI showed a reduction in response to specific therapy [17–19, 21]. Only one study obtained data that contradicted the results of other works. Brown et al. noted an increase in responding lesions on T1-WI after 6–9 months from the start of systemic treatment [18]. In this study, all patients received systemic or local radiotherapy; of these, 17 patients received additional chemotherapy or hormone therapy. The response to therapy in these patients was assessed comprehensively

using clinical, biochemical, radiological, and scintigraphic criteria. The findings might result from the treatment peculiarities that led to the formation of a pronounced and long-term persisting perifocal edema, which gives a hypointense signal on T1-WI leading to false-positive increased sizes of responding lesions according to the practical Met-RADS recommendations [6]. Thus, the dynamics of bone metastasis sizes in response to specific treatment has diagnostic value; however, the result may depend on the time of therapy, different therapeutic approaches and the nature of metastatic lesions. This indicates the necessity for supplementing this criterion with other objective data.

The dynamics of DWI signal intensity could be regarded as an objective criterion for response assessment [5, 16, 20]. The authors of all papers observed a decreased intensity of signal lesion in patients who responded to systemic therapy. However, given that numerical values are presented only in one work [20], and the nature of lesions and type of systemic therapy were not considered in all three papers, further study of the DWI signal intensity change dependence on the aforementioned conditions is necessary.

Determination of numerical ADC values has high potential as an objective assessment criterion and is one of the main ones in the Met-RADS recommendations for the whole-body MRI analysis. Data analysis from seven studies indicated a significant increase in ADC in responding patients [5, 9–12, 16, 20]. Concurrently, all the studies described single cases of ADC decrease with a good response to treatment. These cases were associated with the development of fibrosis or sclerosis in response to therapy. In addition, Messiou et al. demonstrated an increase in ADC in patients with progression; however, these values were less pronounced compared with those in responding patients. Among all seven publications, only one compared ADC values in responding patients with the lesion nature and obtained diverse changes: a 25% increase in ADC in osteoblastic lesions and a 25% decrease in osteolytic lesions [16]. Other studies did not divide lesions into osteolytic and osteoblastic types, thereby resulting in the discrepancy of ADC values in responding patients and clouding the interpretation of these results. These indicate the need for further studies with inclusion of homogeneous groups of lesions.

In studies that assessed tDV, similar results were obtained [11, 12]. They concluded that tDV decreased significantly in response to specific therapy. However, this approach has several limitations. First, these parameters were sensitive to the quality of the DWI, which may lead to tDV changes in the presence of artifacts or insufficient signal reduction by the surrounding tissues. Second, the signal above the 4th–5th cervical vertebrae was manually removed to eliminate a possibly false tDV increase from the brain, salivary glands, and large numbers of lymph nodes, leading to missed lesions in these areas. Third, this method is time-consuming due to a manual processing stage, thereby limiting its widespread use in clinical practice.

Thus, MRI offers a set of objective criteria allowing for the assessment of the efficiency of treating disseminated metastatic skeletal lesions in patients with PC and BC. However, additional studies are required to clarify the methodological aspects and quantitative values of the assessment criteria for different types of metastatic lesions in order to implement widely in clinical practice.

Study limitations

The results of this systematic review call for careful interpretation as we encountered some limitations, such as a small number of included studies, the retrospective nature of some studies, the lack of standardized reference methods, and different types of specific therapy, which may influence the microstructural changes and result in different MR characteristics of responding lesions.

In the reviewed studies and meta-analysis, scanning parameters slightly differ, in particular, different number and values of b-factors are used, which may affect the final ADC values.

CONCLUSIONS

MRI is an informative technique for objective assessment of the response to therapy of bone metastases in patients with PC and BC based on quantitative and semi-quantitative

criteria. Currently, when assessing the treatment efficiency, the dynamics of lesion size in T1 mode and ADC values should be primarily analyzed as precise quantitative assessment criteria have not been developed yet. DWI-based parameters are the most promising; however, this does not exclude the use of traditional RECIST 1.1 and MDA criteria.

Thus, whole-body MRI is a potentially effective diagnostic tool for revealing and monitoring of metastatic skeletal lesions in patients with PC and BC.

ADDITIONAL INFORMATION

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