Research Article

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MRI and bone scintigraphy for breast cancer bone metastase: a meta-analysis

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Abstract: Objective: The aim of this study was to compare the diagnostic value of magnetic resonance image (MRI) and bone scintigraphy (BS) in the diagnosis of breast cancer bone metastases. Methods: Searching in the databases including PubMed, Embase about the comparative study of MRI and bone scintigraphy in the diagnosis of breast cancer bone metastases during 2000~2018. After we screened further, the extracted effective data were calculated by Meta-Disc 1.4 software. Results: We obtained 4 articles. The pooled estimates for sensitivity of MRI, BS were 0.99 (95% CI, [0.95, 1.00]) and 0.93 (95% CI, [0.88, 0.97]) respectively; For specificity were 0.99 (95% CI, [0.95, 1.00]) and 0.86 (95% CI, [0.79, 0.92]) respectively. The AUC of SROC curve for MRI and BS were 0.9948 and 0.9675 respectively. Conclusion: MRI remains to be a satisfactory method for the diagnosis of breast cancer bone metastases and should first be considered for patients.

Keywords: Breast cancer; Bone metastase; Bone scintigraphy (BS); Magnetic resonance image (MRI); Meta-analysis

1 Introduction

Breast cancer is the most common malignant tumor in women, accounting for 23% of all malignant tumors. In recent years, the incidence of breast cancer has increased rapidly, more than 1 million new cases each year worldwide [1]. Bone metastasis occurs in 60% to 70% of recurrence breast cancer patients [2]. Bone metastases cause a series of symptom such as pain, pathological fractures and spinal cord compression, which shortens the survival time from 20 years to 2 years [3]. In addition, bone metastases affect the quality of life of patients. Therefore, accurate and early diagnosis of bone metastasis in breast cancer is of great significance for the treatment and prognosis of breast cancer patients.

At present, the widely used method of bone metastasis screening and examination is bone scan (BS), which has high sensitivity and can obtain images of whole body bone [4], but its specificity is low, and it is easy to cause false positives. Magnetic resonance imaging has the advantages of multi-parameter, multi-azimuth imaging, good soft tissue contrast and high spatial resolution. MRI can clearly distinguish between fat and liquid tissue [5, 6]. With the development of new MRI scanners and coil technology, whole-body diffusion-weighted imaging (WB-DWI) with background body signal suppression, has been recognized as a new imaging modality for the assessment of metastases of various malignancies. MRI has high value in the identification of benign and malignant lesions of the bone [7, 8]. Due to the strong magnetic field of MRI, the examination of patients with metal implants is limited [9], except for WB-DWI, the other MRI techniques can not complete one-time whole body bone imaging compared with bone scan. Therefore, this study collected all the domestic and international MRI and bone scan diagnosis of breast cancer bone metastasis, using meta-analysis to analyze the data, evaluate the diagnostic value of MRI and bone scan for breast cancer bone metastasis, to provide scientific evidence for clinical application.

2 Methods

2.1 Searching method

We conducted a search of PubMed, Embase databases that were published between 2000 and 2018. We limited the search to study published in English. The medical subject heading terms and keywords used included “breast cancer or breast carcinoma or breast neoplasm”, “Osseous metas-

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tases or bone metastases", "magnetic resonance image or MRI", "Bone scan or Bone scintigraphy", "sensitivity and specificity", "diagnoses or diagnosis". According to the specific database, all retrieval strategies are determined by multiple pre-searches. In order to minimize the missing literature, the author also combines manual search and conducts a second search for the references included in the literature.

2.2 Inclusion criteria

Studies were selected carefully on the basis of the following criteria: MRI is compared with gold standards, or bone scans are compared with gold standards for the diagnosis of breast cancer bone metastases. The gold standard is pathological examination and follow-up; Pathologically diagnosed breast cancer, and patients with bone metastases such as bone pain or patients with high degree of suspicion of bone metastases, without limiting age, gender, ethnicity;

2.3 Excluding standard

Non-clinical controlled trials; Non-breast cancer research; Incomplete data; Case reports; Review literature; Data published repeatedly.

2.4 Data extraction

Two authors independently assessed each literature, and then download and extracted all the data by using standardized data-abstraction forms. The data extracted included year of publication, true positive, false positive, false negative, true negative, sensitivity, specificity. For each study, 2×2 contingency tables were constructed. We calculated the sensitivity, specificity, likelihood ratio (LR).

2.5 Statistical analysis

Data analysis was performed using Meta-Disc 1.4 software. Heterogeneity test was performed, and the receiver operating characteristic curve (SROC curve) was drawn and the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic test odds ratio of each diagnostic method were calculated.

3 Results

3.1 Literature searches and characteristics of eligible study

According to search strategy, 4 full articles were finally considered eligible for the review after evaluation. Figure 1 shows the flow diagram of study selection process. The detailed characteristics for the 4 eligible studies are summarized in Table 1.

3.2 Quality assessment

We assessed the quality of the included studies according to QUADAS (10). Each study was evaluated respectively by two independent investigators. On average, the investigators disagreed on 3 of 11 items (range, 0–6). All disagreements were resolved by consensus. The quality evaluation of the included studies is shown in Table 2.

3.3 The diagnostic sensitivity and specificity of MRI

The pooled diagnostic sensitivity and specificity of *MRI* are 0.99 (95% CI, [0.95, 1.00]), 0.99 (95% CI, [0.95, 1.00]) respectively. Significant heterogeneity was found among these studies (I^2=34.5% and 39.3%). Due to significant heterogeneity of the data, we used a random effects model (Figure 2 and 3).

3.4 The diagnostic sensitivity and specificity of BS

The pooled diagnostic sensitivity and specificity of *BS* are 0.93 (95% CI, [0.88, 0.97]), 0.86 (95% CI, [0.79, 0.92]) respectively. Significant heterogeneity was found among these studies (I^2=64.8% and 87.2%). Due to significant heterogeneity of the data, we used a random effects model (Figure 4 and 5).

3.5 The negative LR, positive LR and SROC curve of MRI

The pooled negative LR and positive LR of *MRI* are 0.04 (95% CI, [0.01, 0.12]), 29.36 (95% CI, [8.41, 102.57]) respectively. (Figure 6 and 7). We successfully plotted the SROC

Table 1: Baseline characteristics of included studies

Reference Author	Publication year	MRI				BS			
		TP	FP	FN	TN	TP	FP	FN	TN
Kim (13)	2009	86	0	0	48	87	13	2	32
Engelhard (14)	2004	11	1	1	9	10	2	2	8
Altehoefer (15)	2001	53	0	1	27	47	0	7	27
Layer (16)	1999	5	0	0	28	5	0	0	28

Table 2: Quality assessment of included studies

Included studies	QUADAS													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Kim 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
Engelhard 2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
Altehoefer 2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
Layer 1999	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No

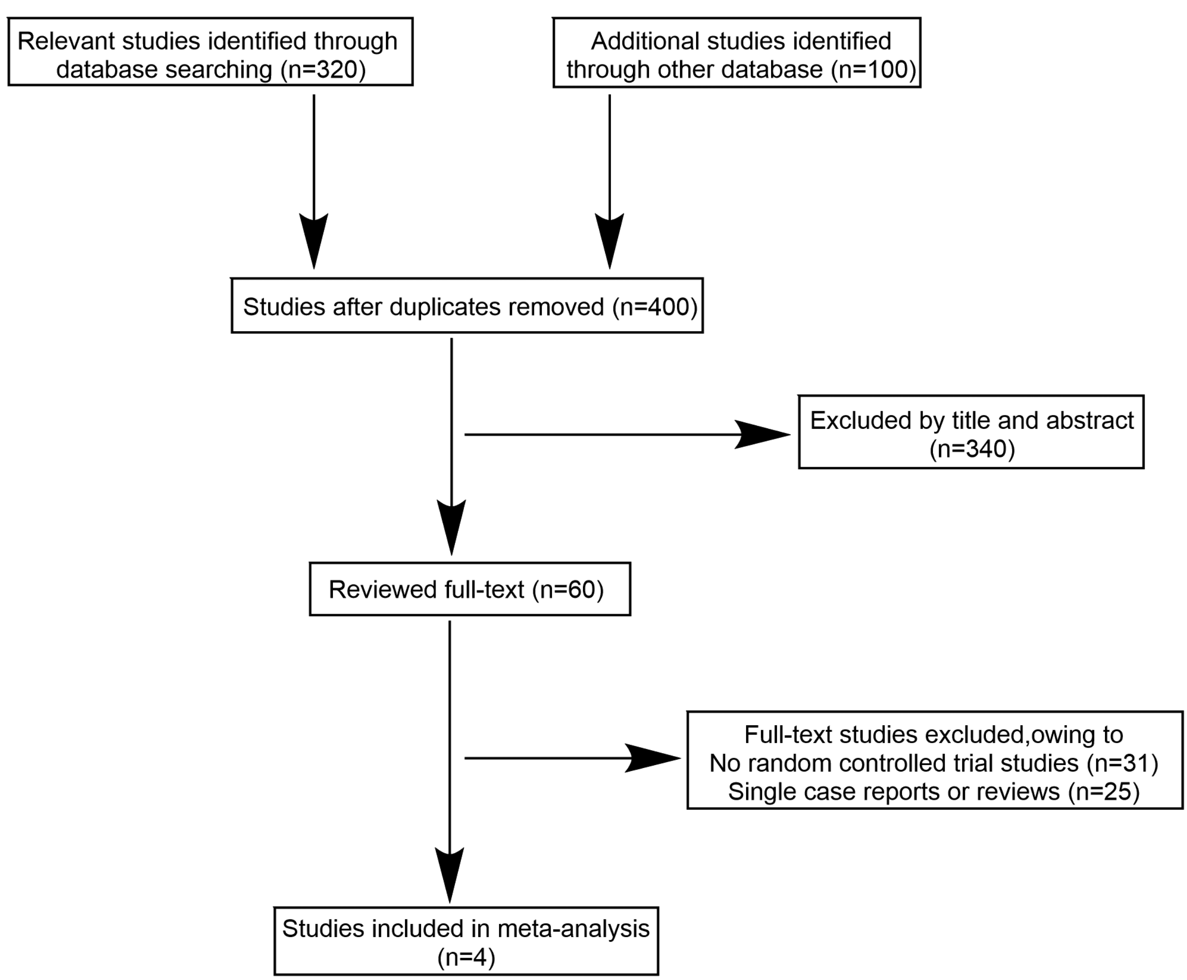

Figure 1: The study selection process

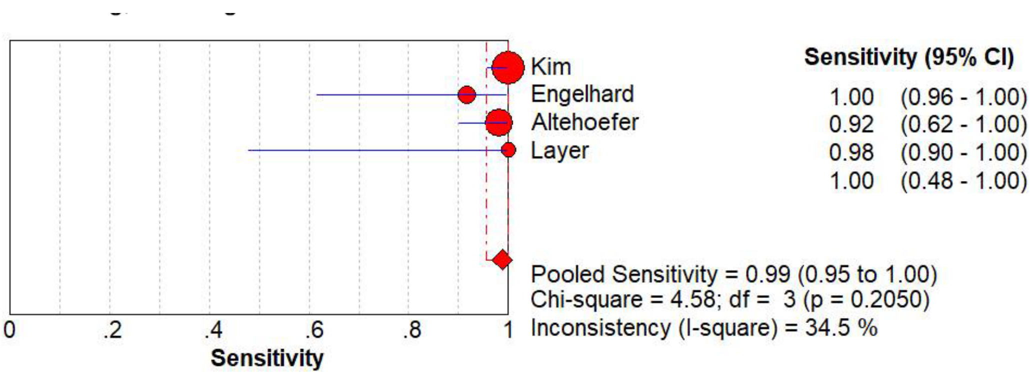

Figure 2: The plot for the sensitivity of MRI

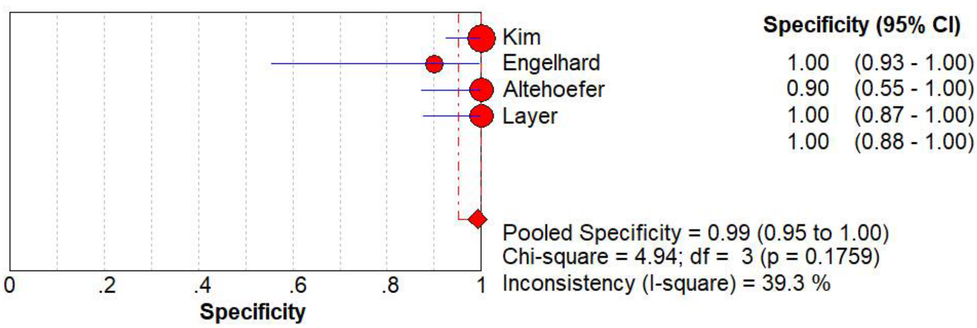

Figure 3: The plot for the specificity of MRI

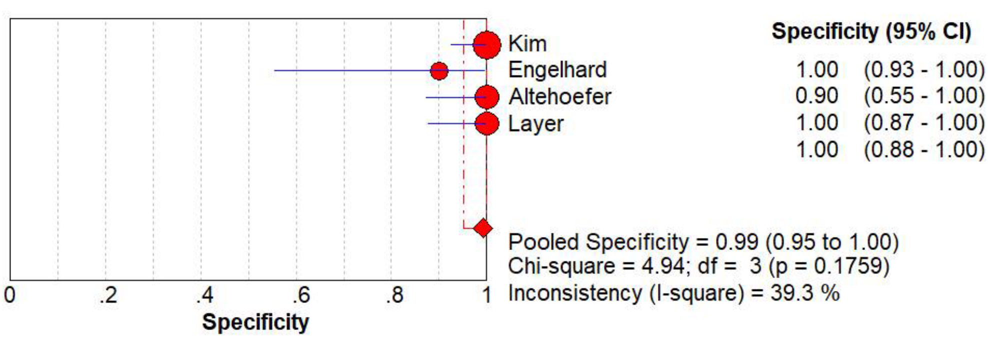

Figure 4: The plot for the sensitivity of BS

curve. The area under the SROC curve (AUC) is 0.9948 and the Q* is 0.9720 (Figure 8).

3.6 The negative LR, positive LR and SROC curve of BS

The pooled negative LR and positive LR of *BS* are 0.10 (95% CI, [0.05, 0.24]), 7.93 (95% CI, [2.17, 28.91]) respectively. (Figure 9 and 10). We successfully plotted the SROC curve. The area under the SROC curve (AUC) is 0.9675 and the Q* is 0.9159 (Figure 11).

4 Discussion

A total of 4 studies were included in this systematic review. Meta-analysis results showed that the combined sensitivity and specificity of MRI for the diagnosis of breast cancer with bone metastases were 99%, indicating that the rate of missed diagnosis and misdiagnosis was very low (1%); the area under the curve of MRI and bone scan was 0.9948 and 0.9675, their diagnostic performance are high. The combined sensitivity of bone scan for the diagnosis of breast cancer with bone metastases was 93%, indicating a missed diagnosis rate of 7%; combined specificity was 86%, indicating a misdiagnosis rate of 14%. Therefore,

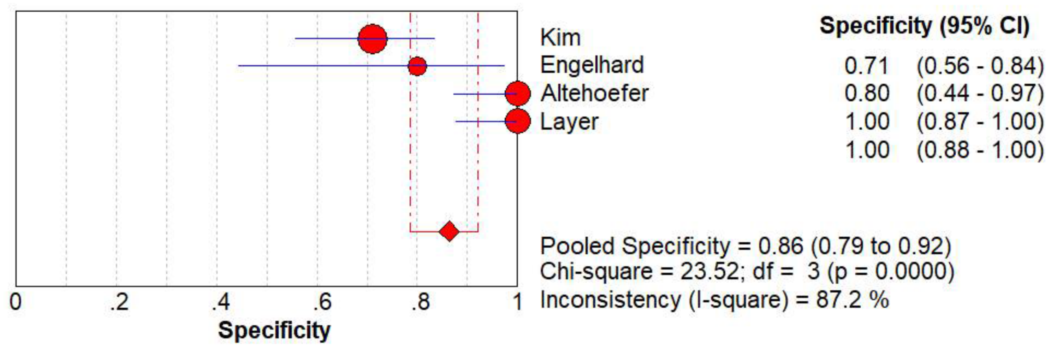

Figure 5: The plot for the specificity of BS

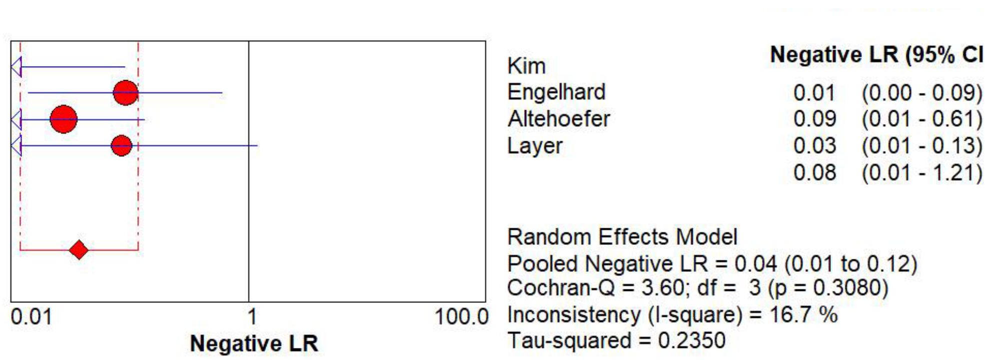

Figure 6: The plot for the negative LR of MRI

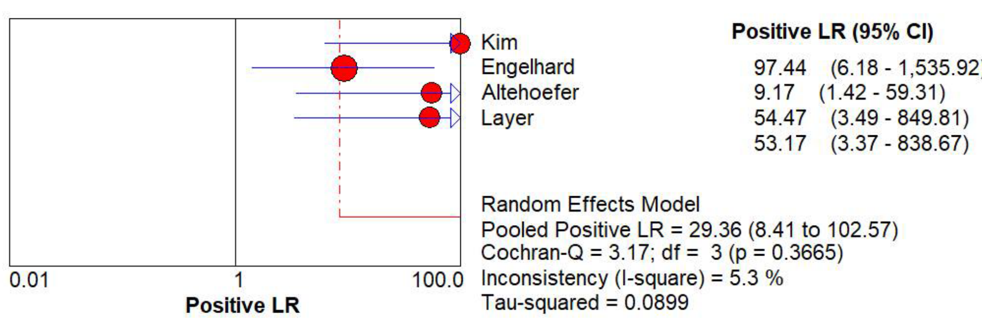

Figure 7: The plot for the positive LR of MRI

compared with bone scan, the missed diagnosis rate and misdiagnosis rate of MRI in the diagnosis of breast cancer bone metastasis are very low, and the SROC curve of MRI is close to the upper left corner, that is, the area under the curve is larger, indicating the accuracy of MRI for bone metastasis of breast cancer. Higher, combined with MRI's image quality is high. Therefore, MRI is a more accurate method for diagnosing bone metastasis in breast cancer.

The 4 studies included in this systematic review were from different countries, and the combination of computer and manual search was used in the search process, and the data collection was relatively comprehensive. In the diagnosis of diseases, the diagnosis results of MRI and bone scan are related to the severity of the disease and the diagnostic level of doctor. However, all included studies do not describe such problems, which may influence the interpretation of the results. Due to included studies were lack of negative trials, there may be potential publish bias, although it was reported that the low detection rate and high cost of MRI is little value for diagnosis of breast cancer bone metastases [11].

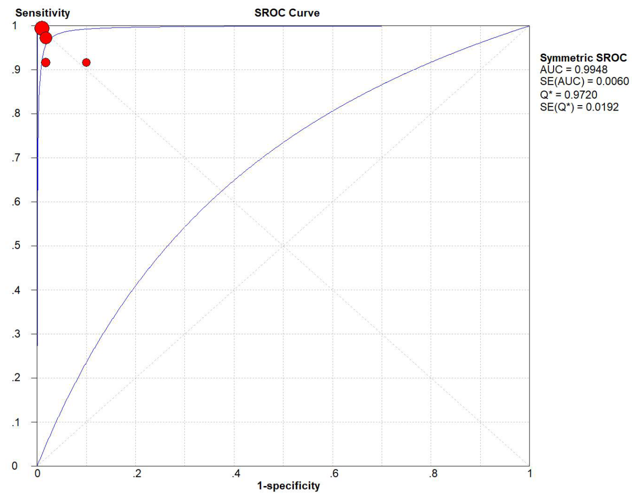

Figure 8: The SROC curve of MRI

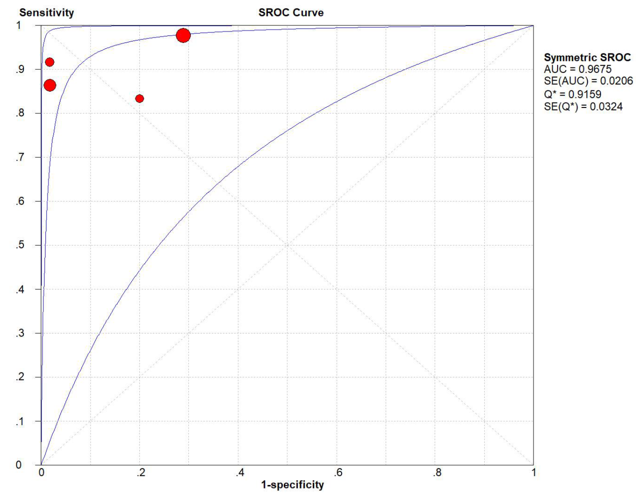

Figure 11: TThe SROC curve of BS

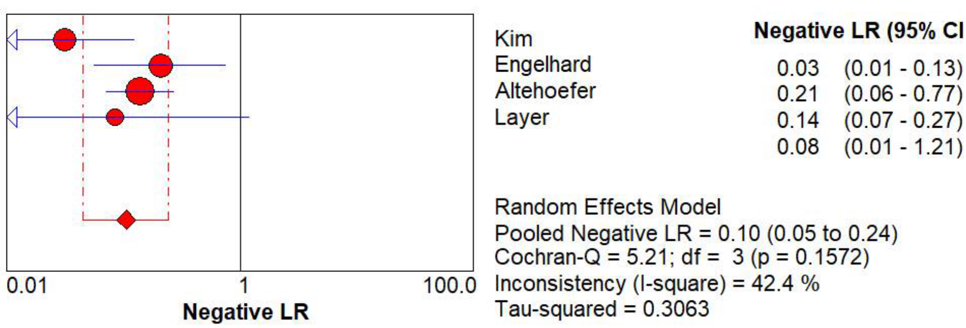

Figure 9: The plot for the specificity of MRI

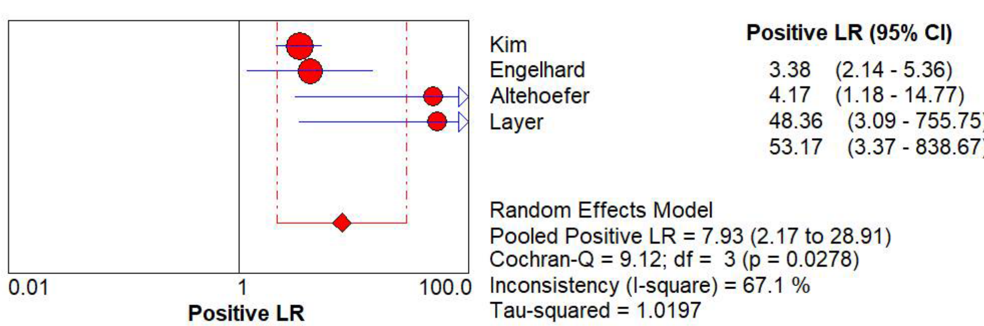

Figure 10: The plot for the sensitivity of BS

In this study, as long as there is a metastasis, there is a positive case. If the same patient has multiple metastases, the number of lesions detected by MRI and bone scan is different from the difference between the good and the malignant. Bone scans sometimes show multiple abnormal uptake areas, but both benign and malignant lesions coexist, and it is not possible to clearly distinguish between benign and malignant specific lesions [12]. The advantages of MRI are multi-azimuth imaging and multi-sequence multi-parameter imaging, with high specificity and high quality images. In recent years, the PET-like technique, magnetic resonance systemic diffusion-weighted imaging (WB-DWI), has a very high sensitivity to malignant tumor examination, and can obtain system-specific tumor imaging similar to PET. Inspection costs are much lower than PET and are widely used in clinical practice [8].

In summary, MRI can be an effective and feasible method for diagnosing bone metastasis in breast cancer. However, the limitations of methodology, high-quality studies are needed to further confirm the clinical value of MRI in the diagnosis of breast cancer bone metastasis.

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