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ARAŞTIRMA / RESEARCH

Kemik metastazlarının saptanmasında kemik sintigrafisi ve tüm vücut difüzyon manyetik rezonans görüntülemenin karşılaştırılması

Comparison of bone scintigraphy and whole-body diffusion-weighted magnetic resonance imaging in the detection of bone metastases

Sinan Sözütok[1], Serdar Tarhan[1], Fatih Düzgün[1], Elvan S. Bilgin[2]

[1]Manisa Celal Bayar University Faculty of Medicine, Department of Radiodiagnostic, [2]Department of Nuclear Medicine, Manisa, Turkey

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Abstract

Purpose: The aim of this study was o evaluate the efficacy and success of whole-body diffusion-weighted magnetic resonance imaging (WB-DW-MRI) as a new method for the detection of bone metastasis commonly seen in malignancies, compared to bone scintigraphy.
Materials and Methods: The WB-DW-MRI findings of 21 patients with primary malignancies and bone metastases were retrospectively evaluated and compared to scintigraphy findings.
Results: Twenty-one patients had 143 metastatic lesions detected by scintigraphy, and 96 of these bone metastases were also detected on WB-DW-MRI. The area where the success of WB-DW-MRI was highest was the lower extremities, for which 12 (92.3%) of 13 metastases were identified. This was followed by vertebrae, for which WB-DW-MRI detected 39 (86.6%) of 45 metastases. The metastasis detection rates for the upper extremities, pelvis, and cranium were calculated as 73.6%, 63.1%, and 60%, respectively. WB-DW-MRI was least successful in identifying metastases in ribs, with only 16 (38.1%) of 42 metastases being detected by this modality.
Conclusion: In line with the findings obtained from this study, it is considered that WB-DW-MRI may be successful in the detection of bone metastases, especially in the axial skeleton. The failure observed for the ribs can be remedied by newly developed magnetic sensitivity technologies, increasing geometric resolution, and fast sequences that will prevent motion artifacts.

Keywords:. bone metastases, whole-body diffusion MRI, bone scintigraphy

Öz

Amaç: Bu çalışmanın amacı malignitelerde yaygın olarak görülen kemik metastazının saptanmasında yeni bir yöntem olarak tüm vücut difüzyon ağırlıklı manyetik rezonans görüntülemenin (TVDAMRG) etkinliğini ve başarısını kemik sintigrafisi ile karşılaştırarak değerlendirmektir.
Gereç ve Yöntem: Primer malignitesi ve kemik metastazları olan toplam 21 hastanın tüm vücut difüzyon MRG (manyetik rezonans görüntüleme) bulguları retrospektif olarak değerlendirilmiş ve bulgular kemik sintigrafisi ile karşılaştırılmıştır.
Bulgular: 21 hastada kemik sintigrafisiyle saptanan toplam 143 metastatik lezyon mevcuttur. Saptanan 143 kemik metastazından 96 tanesi difüzyon MRG'de de tespit edilebilmiştir. Difüzyon MRG'nin tespit başarısının en yüksek olduğu bölge alt ekstremiteler olmuştur ve 13 metastazın 12'sini %92.3'lük oranla tespit edebilmiştir. Vertebralar diğer başarılı olunan bölge olup 45 metastazın 39'u difüzyon MRG'de de izlenebilmiştir. Başarı yüzdesi %86.6 dır. Üst ekstremite, pelvis ve kranial bölgelerdeki saptama oranı sırasıyla %73.6, %63.1 ve %60 olarak hesaplanmıştır. En başarısız bölge ise kostalar olmuştur. Kostalarda mevcut olan 42 metastazın sadece 16'sı tespit edilebilmiş olup saptama yüzdesi %38.1'dir.
Sonuç: Çalışmamızda elde ettiğimiz bulgular doğrultusunda tüm vücut difüzyon MR görüntülemenin kemik metastazlarının tespitinde özellikle aksiyal iskelette başarılı olabileceği düşünülmüştür. Kostalardaki başarısızlık oranı yeni geliştirilecek manyetik duyarlılık teknolojileri, artırılan geometrik rezolüsyon ve hareket artefaktını engelleyecek hızlı sekanslar sayesinde düzeltilebilir.

Anahtar kelimeler: kemik metastazları, tüm vücut difüzyon MRG, kemik sintigrafisi

Yazışma Adresi/Address for Correspondence: Dr. Sinan Sözütok, Manisa Celal Bayar University Faculty of Medicine. Department of Radiodiagnostic, Manisa, Turkey E-mail: sozutoks@yahoo.com
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INTRODUCTION

Cancer, which has an increasing incidence in Turkey, as well as all over the world, is an important health problem that ranks first among causes of adult deaths in both developed and developing countries. There are many variables in determining the prognosis of the disease and possible treatments, and one of the most important variable is metastases. Bone tissue is one of the locations where metastases are frequently seen, and bones are involved in 20-35% of other organ cancers, except for the primary malignancies of the skeleton[1].

Metastatic bone tumors are the most common neoplastic lesions of the skeletal system, and 65% of patients with advanced cancer have bone metastases[2]. Among distant metastases, bone metastases are the third most common after those of the lung and liver. They are mostly seen in young people and adults, and rarely develop in childhood. Bone metastases occur in the axial skeleton at a rate of 80%, cranium at 10%, and long bones at 10%. The bones metastasized by tumors are reported, in order of frequency, as vertebrae (45%), pelvis and sacrum (20%), femur and ribs (15%), skull and humerus (9%), scapula and sternum (5%), clavicle (4%), and tibia (2%) (3,4). When all bone metastases are evaluated, it is seen that more than 80% consist of breast, prostate, lung, kidney and thyroid cancers. Bone metastases are most commonly observed in prostate cancer in men and breast cancer in women[3-5].

Positron emission tomography (PET), PET-computed tomography (PET-CT), and scintigraphy are frequently used nuclear medicine imaging methods for screening and determining bone metastases. However, these examinations have certain disadvantages, such as high ionizing radiation exposure, variations in 18-fluorodeoxyglucose (18-FDG) physiology, and scanning artifacts[6-7]. The use of diffusion-weighted magnetic resonance imaging (DW-MRI) in the evaluation of oncological diseases is increasing day by day[8].

The high cellularity that constitutes the pathophysiology of malignancies and the consequent decrease in water molecule diffusion at extracellular distance allows the use of DW-MRI in the imaging of oncological patients[9-10]. MRI not containing ionizing radiation and having high soft tissue resolution are among the characteristics preferred by clinicians in staging and screening processes. Along with the advances in MRI technology, the use of mobile patient platforms integrated with the surface coil technology also enabled the whole body to be imaged in a single session[11-14].

Studies show that whole-body DW-MRI (WB-DW-MRI) has higher sensitivity in detecting bone metastases compared to PET-CT and scintigraphy[15-23]. In addition, in terms of providing information about multisystemic involvement, MRI has become a non-radiation alternative to routine screening techniques[24]. In this study, both examinations were compared in order to determine the appropriateness of using WB-DW-MRI, which is an easier and non-radioactive method instead of scintigraphy.

MATERIALS AND METHODS

For this study, ethics committee approval was obtained by the Clinical Research Ethics Committee of Celal Bayar University School of Medicine (Date: 25.02.2015, decision number: 20478486-93). The institute in which the study was conducted was a university hospital, and the necessary records for the study were obtained safely in both oncology and radiology departments. In the evaluation, the cancer histories and radiological report records of the patients were carefully questioned, and the information obtained was recorded accurately by the authors in a way that would not cause bias. The patient name, age, clinical histories, and radiological findings were noted on the forms in which information was obtained from the patients.

Sample

In this study, the WB-DW-MRI images of patients, who were followed up at Celal Bayar University Faculty of Medicine Hafsa Sultan Hospital due to primary malignancies and had bone metastasis detected on scintigraphy, were retrospectively evaluated for the scans undertaken between January 2011 and November 2014 and compared with bone scintigraphy findings.

A total of 21 patients, 17 males and four females, were included in the study. The ages of the patients varied between 49 and 82 years, and the mean age was calculated as 67.3 years. Three of the female patients were followed up with a diagnosis of breast cancer (invasive ductal carcinoma) and one with renal cancer (renal cell adenocarcinoma) while all the male patients had been diagnosed with prostate cancer (adenocarcinoma).

The bone metastases of the patients were confirmed by CT, MRI and PET-CT obtained during their follow-up, and there were no histopathological diagnoses for bone metastases. Patients with more than 30 days between WB-DW-MRI and scintigraphy scans were not included in the study. However, since this period was exceeded in any of the selected patients, all of them were included in the study. Apart from this, there were no specific criteria for patient exclusion, and all cancer patients with bone metastases and who could undergo scintigraphy with MRI were included in the study.

Table 1. Technical parameters of the MRI sequences

	Axial diffusion	Coronal STIR
TR	5750 msn	3.0-15000 msn automatic detection
TE	81.4 msn	34 msn
FOV	42 cm	48 cm
Matrix	92x128	288x160
Section thickness	8 mm	10 mm
Section interval	0 mm	2 mm

TR: Time to repeat, TE: Time to echo, FOV: Field of view, STIR: Short-tau inversion recovery

MRI protocol

The MRI examinations of all patients were obtained using a GE SIGNA 1.5 T MRI device. Diffusion images were obtained in six stations as head, neck-upper thorax, lower thorax-upper abdomen, upper abdomen-lower abdomen, pelvis-thigh, and below knee for the axial plane, and four stations, namely head-neck-upper thorax, lower thorax-upper abdomen, lower abdomen-proximal thigh, and distal thigh-below knee. MRI was performed using a body coil with patients placed in a supine position, entering the gantry feet first. Contrast agent was not used. The duration of the examination varied depending on the patient's height, but was completed in 26 minutes on average. Axial diffusion EPI and coronal short-tau inversion recovery (STIR) sequences were used in the examination. The sequence parameters are given in Table 1. Diffusion-weighted images were evaluated with the b-1000 value. No custom apparent diffusion coefficient (ADC) value was selected.

Scintigraphy protocol

Bone scintigraphy was performed using a GE INFINIA GP3 double-detector gamma camera device equipped with low-energy and high-resolution collimators. The images were obtained approximately three hours after an intravenous infusion of 925 MBq Tc99m MDP (methylene diphosphoric acid) at 140 keV energy peak of Tc^{99m} with a 20% window width. A 1024x256 matrix was used for image formation. The duration of the examination varied according to the patient's height, and the mean exposure time for each pixel was 180 seconds. No premedication was given to the patients, and the patients were hydrated after the examination.

Evaluation

The WB-DW-MRI and scintigraphy images were evaluated independently using dedicated workstations, then the lesions found were compared and the sensitivity of WB-DW-MRI was measured according to the bone scintigraphy used as reference. Reformatted MPR coronal images were created from the obtained axial WB-DW-MRI images and evaluated together with coronal STIR images. Areas with a high signal in STIR sequences and showing significant diffusion restriction in diffusion images were accepted as metastases. Symmetrical and diffuse involvements were primarily evaluated as bone marrow reconversion in patients receiving chemotherapy. Since normal structures and benign lesions can also have false positive results in DW images, the conventional examinations of the patients were used for the exclusion of these structures.

Statistical analysis

The Kolmogorov-Smirnov test was used to determine whether the groups were normally distributed. The Spearman correlation analysis was conducted since the groups did not have a normal distribution. P values of <0.05 were considered statistically significant. All statistical analyses were undertaken using in SPSS v. 15.0.

RESULTS

Twenty-one patients had 143 metastatic lesions detected by bone scintigraphy. The images of some of the metastatic lesions are shown in Figures 1 to 3. Forty-five metastases were detected in vertebrae, 19 in pelvis, 42 in ribs, 19 in upper extremities, 13 in lower extremities, and five in cranial bone structures. Ninety-six of the 143 bone metastases detected by scintigraphy were also identified by WB-DW-MRI. The latter was most successful in the detection of metastases located in the lower extremities, for which 12 of 13 metastases were identified (92.3%). We detected 39 of 45 metastases in vertebrae (86.6%) using WB-DW-MRI. The area where the least number of metastases was detected by WB-DW-MRI was the ribs, with only 16 of 42 metastases (38.1%) being successfully identified. Table 2 presents the data on the metastasis detection rates of scintigraphy and WB-DW-MRI.

Table 2. Distribution of metastases detected by scintigraphy and diffusion MRI by body area

	Cranial		Vertebrae		Ribs		Pelvis		Lower ext.		Upper ext.		Total	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D
Case 1	-	-	-	-	-	-	1	1	-	-	1	-	2	1
Case 2	-	-	1	1	5	1	4	-	-	-	1	1	11	3
Case 3	-	-	-	-	4	-	2	-	-	-	1	-	7	0
Case 4	-	-	1	-	2	-	-	-	-	-	1	-	4	0
Case 5	1	-	2	-	-	-	-	-	-	-	-	-	3	0
Case 6	-	-	1	1	4	-	1	-	2	2	2	1	10	4
Case 7	-	-	2	-	3	-	3	3	1	1	-	-	9	4
Case 8	-	-	-	-	2	-	2	2	1	1	-	-	5	3
Case 9	-	-	1	-	2	2	-	-	-	-	1	-	4	2
Case 10	1	1	10	10	-	-	1	1	1	1	4	4	17	17
Case 11	-	-	-	-	-	-	1	1	1	1	2	2	4	4
Case 12	1	1	2	2	2	2	-	-	1	1	1	1	7	7
Case 13	-	-	-	-	2	-	-	-	-	-	-	-	2	0
Case 14	-	-	10	10	3	-	1	1	2	2	-	-	16	13
Case 15	-	-	1	1	-	-	1	1	-	-	-	-	2	2
Case 16	1	1	10	10	5	5	-	-	2	2	4	4	22	22
Case 17	1	-	-	-	4	3	1	1	1	1	1	1	8	6
Case 18	-	-	-	-	1	1	-	-	1	-	-	-	2	1
Case 19	-	-	2	2	-	-	-	-	-	-	-	-	2	2
Case 20	-	-	1	1	2	2	-	-	-	-	-	-	3	3
Case 21	-	-	1	1	1	-	1	1	-	-	-	-	3	2
Total	5	3	45	39	42	16	19	12	13	12	19	14	143	96

S: scintigraphy, D: diffusion MRI

Figure 1. A 62-year-old woman with breast cancer. Increased Tc-99m involvement in the right seventh rib on bone scintigraphy and hyperintensity of diffusion restriction on axial diffusion MRI.

Table 3. Statistical results of the pelvic and rib lesions

Correlation analysis for the pelvis			**S, Ribs**	**D, Ribs**	
Spearman's rho	Scintigraphy Kosta	Correlation Coefficient	1,000	0.095	**No correlation between scintigraphy and diffusion MRI findings for the metastases detected.
		Sig. (2-tailed)	.	0.683	
		N	21	21	
	Diff. MRI Ribs	Correlation Coefficient	0.095	1.000	
		Sig. (2-tailed)	0.683	.	
		N	21	21	
Correlation analysis for the pelvis			S, Pelvis	D, Pelvis	
Spearman's rho	Scintigraphy Pelvis	Correlation Coefficient	1.000	0.629(**)	**Correlation is significant at the 0.01 level (2-tailed).
		Sig. (2-tailed)	.	0.002	
		N	21	21	
	Diff. MRI Pelvis	Correlation Coefficient	0.629(**)	1.000	
		Sig. (2-tailed)	0.002	.	
		N	21	21	

S: scintigraphy, D: diffusion MRI, p ≤ 0.05: statistically significant; Correlation coefficient: 0.70 – 1.00: high, 0.70 – 0.30: moderate, 0.30 – 0.00: low

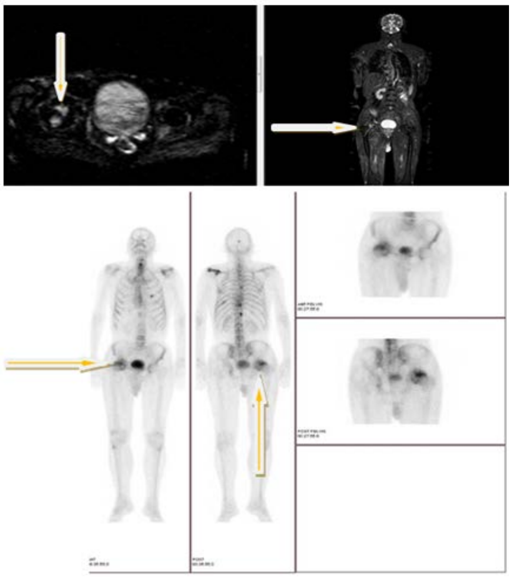

Figure 2. A 73-year-old male patient with prostate cancer. Increased Tc-99m involvement in the right femoral head on bone scintigraphy, and hyperintensity of diffusion restriction in the same localization in coronal STIR images and axial plane on whole-body diffusion MRI.

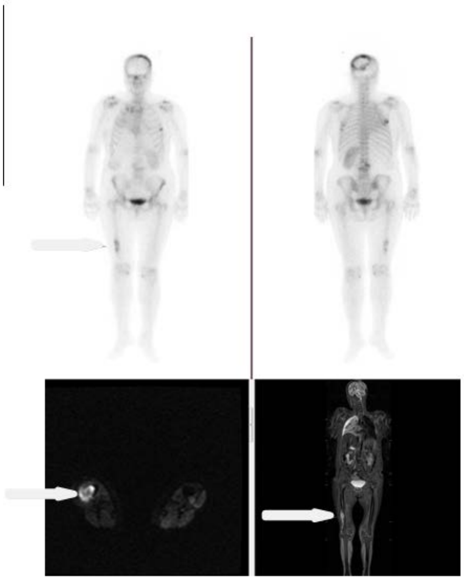

Figure 3. A 49-year-old woman with renal cancer. Increased Tc-99m involvement in the right femur distal diaphysis on bone scintigraphy, and hyperintensity of diffusion restriction in the same localization in coronal STIR and axial diffusion images.

The Spearman correlation analysis between the two methods revealed a high level of positive correlations for the cranial, vertebrae, and upper and lower extremities. There was a moderate positive correlation for the pelvis and no correlation for the ribs. The results of the statistical evaluation for the pelvic and rib lesions are given in Table 3. In addition to existing metastases, there were asymmetric local areas incompatible with bone marrow reconversion that were not evaluated as metastasis on bone scintigraphy but showed diffusion restriction on MRI. These areas were located in the femur proximal diaphysis in Case 5, vertebra corpus (multiple) in Case 7, right sacrum and right acetabulum in Case 21, and L1 vertebra corpus in Case 21. No pathological diagnosis was made for these areas.

DISCUSSION

Distant organ metastases are important variables in determining prognosis and treatment options in patients with malignancies. Bone tissue involvement is one of the most common metastasis localizations seen in 20-35% of organ cancers other than the primary malignancies of the skeleton. The vast majority of bone metastases occur due to hematological spread and are observed in the bone marrow as micrometastases in 25-75% of cases. Despite differing according to the type of malignancy, the most common areas of metastasis are the axial skeleton, such as vertebrae, pelvis, skull, ribs, and proximal femur detected as the localization of metastasis in 70% of patients[25].

PET-CT is the most commonly used method in routine applications for the evaluation of all distant metastases. Another specific examination used for bone metastases is bone scintigraphy. Although the success rates of these two tests in detecting metastases are very high, the amount of radiation received by the patient, the side effects caused by radioactive substances applied or the effects of radiation exposure create restrictions in the use of these tests. Therefore, for the detection of distant metastases, higher diagnostic and more practical imaging techniques are evaluated as an alternative to PET-CT and scintigraphy. In the studies conducted, diffusion MRI provides satisfactory results in metastasis detection and screening. Diffusion MRI not containing ionizing radiation is one of the favorable characteristics that makes it preferable in staging and screening. In addition, its ability to show metastases of solid organs included in the examination enables a systemic evaluation[26].

In the literature, there are studies comparing WB-DW-MRI and bone scintigraphy. In a study by Del Vescovo et al., WB-DW-MRI, bone scintigraphy and CT survey were compared. In that study, conventional MRI was chosen as the gold standard. According to the results, diffusion MRI detected 20% more metastases than scintigraphy and 119% more than CT. As in our study, the authors reported that the localizations where diffusion MRI was most effective were the axial skeleton and extremities while this modality failed to accurately detect metastases in the ribs. The authors concluded that although diffusion MRI was highly sensitive, bone scintigraphy was a more specific method[27].

In a study comparing conventional MRI, WB-DW-MRI, bone scintigraphy, and PET-CT in the detection of bone metastases of small cell lung cancer, it was revealed that bone scintigraphy and PET-CT were more specific in the diagnosis of bone metastases. However, conventional MRI with diffusion sequences was found to have the highest sensitivity, and conventional MRI with diffusion MRI sequences was more sensitive than conventional MRI without diffusion sequences[28].

In a study by Goudarzi et al., diffusion MRI, bone scintigraphy, and PET-CT were compared by taking conventional MRI as the gold standard. In that study, diffusion MRI detected 92.3% of lesions, bone scintigraphy 23.1%, and PET-CT 56.5%. It was observed that diffusion MRI had a higher rate of detection of small lesions; however, benign lesions and normal structures were also seen with high signals due to the T2 shine-through effect, which resulted in false positive findings. As our results also reflected, the authors of the previous study emphasized that a diffusion MRI evaluation to which conventional sequences are added would be more successful[24].

Costelloe et al., who compared WB-DW-MRI with scintigraphy using conventional MRI as the gold standard, reported that in detecting bone metastases, diffusion MRI was more sensitive with a sensitivity value of 70.8% and bone scintigraphy was more specific with a specificity value of 98.7%. Similar to our findings, the author noted that the success of diffusion MRI was very high in detecting metastases located in the axial skeleton and extremities[29].

In a study comparing diffusion MRI with bone scintigraphy using one-year clinical follow-up and other additional tests as the gold standard, the sensitivity of diffusion MRI in detecting bone metastases (96.5%) was higher than that of scintigraphy[30].

In the meta-analysis of 11 studies in the literature, it was stated that diffusion MRI was highly sensitive but had specificity in the diagnosis of bone metastases[31].

In another research study, the high sensitivity of diffusion MRI was attributed to its ability to show malignant cells located in that area, and its superiority in detecting small lesions was associated with the detection of malignant metastases in these localizations long before they caused remodeling and pathological FDG involvement[32].

In most studies in the literature, conventional MRI was used as the gold standard, and the histopathological diagnosis of the detected metastases was not made. Accordingly, although diffusion MRI stands out as a more sensitive test compared to other examinations, due to the absence of histopathological examinations in studies conducted, the accuracy of this sensitivity can only be confirmed by further studies including pathological diagnoses based on biopsies. Since we used bone scintigraphy in our study, which is a more specific test as also reported by previous researchers, it was not possible to obtain higher sensitivity and specificity for WB-DW-MRI.

In this study, the high rate of WB-DW-MRI in the detection of the metastases of the axial skeleton is consistent with other studies in the literature, and we also observed that the bones in the areas, such as the vertebra and pelvis were very compatible with diffusion imaging due to their immobile fixed structures. In addition, due to the resolution of large bone structures and easier differentiation of the surrounding soft tissues, bone-soft tissue separation and anatomical localization could be performed with more precision.

The area where diffusion MRI was most unsuccessful was the ribs, and the failure of this modality for this area was the major reason for the low number of metastases detected by diffusion MRI in our study. The reason for this failure was considered to be geometrical distortion artifacts and signal loss due to changes in magnetic sensitivity in tissues close to the lungs. In addition, due to the relatively thin and small volume structures of the ribs, it was difficult to anatomically distinguish metastases from the surrounding soft tissues by diffusion MRI with low spatial resolution. With the addition of respiratory motion artifacts, the rib metastasis detection rate of diffusion MRI was considerably decreased.

In a study conducted by Nemeth et al., it was revealed that diffusion MRI was more successful than in detecting bone metastases of breast and lung cancers than sclerotic metastases of prostate cancer[33]. The authors consider the reason for this to be sclerotic metastases containing fewer mobile protons. In our study, a large number of patients were diagnosed with prostate cancer, which can also explain our reduced rate of metastasis detection by diffusion MRI compared to other studies.

In our study, the most important limitation in the evaluation of the images was the monitoring of normal structures or benign lesions with high intensity in diffusion sequences due to the T2 shine-through effect. The MRI protocol we used consisted of coronal STIR and axial EPI diffusion sequences. T1-weighted (T1W) images used in conventional MRI are important in the evaluation of existing bone pathologies, especially bone marrow edema. It is clear that in cases where the bone pathologies of many benign features, such as degenerative changes, fractures, edema, infection, hemangioma, and bone marrow reactivation due to the treatment received are observed with bright signal intensity in diffusion MRI and STIR sequences, the false positive rate will increase if T1A sequences are not included in the scanning protocol. The necessity of supporting diffusion imaging by T1A sequences was also emphasized by Wilhelm et al.[26]. However, each added sequence prolongs the examination period, causing problems in patients with a poor general state of health and cannot tolerate a long scanning procedure.

Another limitation of this study was the low patient compliance. In the presence of malignancies accompanied by general condition disorder, the difficulty of monitoring the patients in the MRI device and the inability to establish sufficient cooperation with the patient result in non-diagnostic images to be obtained in diffusion sequences that are considerably affected by movement. Furthermore, patients having extensive pain due to bone metastases makes it difficult for them to tolerate the examination in the claustrophobic environment created by the MRI device. Compared to the durations of scintigraphy and PET-CT ranging from 20 to 30 minutes, MRI imaging, which can take up to 50-60 minutes with additional sequences, is seen as a difficult examination to be tolerated by patients.Our results reveal that WB-DW-MRI is successful in the detection of bone metastasis, especially in the axial skeleton. However, this imaging modality did not have the same success in areas of motion artifacts. The failure rate of this modality in the detection of rib metastases can be reduced by newly developed magnetic sensitivity technologies, increased geometric resolution, and fast sequences that prevent motion artifacts. Due to the difficulties in application, the use of WB-DW-MRI in routine practice may not be possible until the scanning time is significantly reduced. There is also a need for prospective studies conducted with a higher number of patients with a variety of malignancies.

Yazar Katkıları: Çalışma konsepti/Tasarımı: ST, ESB, FD, SS; Veri toplama: SS, FD; Veri analizi ve yorumlama: SS; Yazı taslağı: SS; İçeriğin eleştirel incelenmesi: ST, ESB, FD, SS; Son onay ve sorumluluk: SS, ST, FD, ESB; Teknik ve malzeme desteği: SS; Süpervizyon: ST, FD; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Celal Bayar Üniversitesi Tıp Fakültesi Yerel Etik Kurulundan 16.02.2015 tarih ve 74 sayılı kararı ile etik onay alınmıştır.
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