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# In Vivo and In Vitro Studies of the Steady State Free Precession-Diffusion-Weighted MR Imagings on Low b-value : Validation and Application to Bone Marrow Pathology*

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## -Abstract-

**Purpose** : The purpose of this study was a phantom study to measure the diffusion properties of water molecules by steady-state free precession diffusion-weighted imaging (SSFP- DWI) with a low b-value and to determine if this sequence might be useful for application to the evaluation of bone marrow pathology.

**Materials and methods** : 1. The phantom study:

A phantom study using two diffusion weighted sequences for the evaluation of the diffusion coefficient was performed. Three water-containing cylinders at different temperatures were designed: phantom A was 3℃, B was 23℃ and C was 63℃. Both SSFP and echo planar imaging (EPI) sequences (b-value: 1000 s/mm$^2$) were performed for comparison of the diffusion properties. The Signal to noise ratios (SNR) and apparent diffusion coefficient (ADC) values of the three phantoms using each diffusion-weighted sequence were assessed.

2. The Clinical study:

SSFP-DWI was performed in 28 patients [sacral insufficiency fractures (10), osteoporotic lumbar compression fractures (10), malignant compression fractures (8)]. To measure the ADC maps, a diffusion-weighted single shot stimulated echo-acquisition mode sequence (650s/ mm$^2$) was obtained using the same 1.5-T MR imager

**Results** : For the phantom study, the signal intensity on the SSFP as well as the classic EPI-based DWI was decreased as the temperature increased in phantom A to C. The ADC

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values of the phantoms on EPI-DWI were $0.13\times10^{-3}$ $mm^2/s$ in phantom A, $0.22\times10^{-3}$ $mm^2/s$ in B and $0.37\times10^{-3}$ $mm^2/s$. in C. The SSFP can be regarded as a DWI sequence in view of the series of signal decreases.

**Conclusion** : Bone marrow pathologies with different diffusion coefficients were evaluated by SSFP-DWI. All benign fractures were hypointense compared to the adjacent normal bone marrow where as the malignant fractures were hyperintense compared to the adjacent normal bone marrow.

**Key Words**: Spine, Compression fracture, Diffusion MR

## Introduction

Diffusion-weighted magnetic resonance imaging (DWI) has become widely available and used in clinical medicine. With this technique the mobility of tissue water can be measured in vivo on microscopic levels. Changes of the motion of water molecules in tissue can be detected in diverse pathological conditions. In the neuroradiology setting, DWI is already a well-established method that has proved to be an especially useful assessment modality for acute stroke.[1-3] DWI for the brain imaging primarily uses echo planar imaging sequences (EPI). This technique has not been successfully applied to the bone marrow pathology because of its susceptibility artifacts. In this study, the diffusion-weighted imaging sequence was based on a steady-state free precession (SSFP). For this sequence type, the b value cannot easily be quantified and there is no simple way to determine the apparent diffusion coefficient (ADC) by SSFP diffusion sequences.[4] Diffusion weighting (or the b value) of this sequence is low. Therefore, evaluation of the changes of the mobility of water molecules in vitro on a microscopic level, might be achieved by analyzing these sequences by comparing the signal change such as the signal to noise ratio and the ADC of this sequence with that of the EPI-based DWI.

Conventional spin-echo sequence MR imaging is very sensitive for the detection of pathological lesions in the bone marrow. However, the differential findings between spinal benign compression fractures and malignant tumor induced spinal compression fractures are often not obvious because of the nonspecific changes of the signal intensity. Recently, there have been several reports on the usefulness of DWI for the differentiation of malignant and benign vertebral compression fractures.[5-8] Therefore, the purpose of this study was to perform a phantom study to determine the diffusion properties of SSFP-DWI with a low b-value and to investigate whether if this sequence would be useful for

the diagnosis of bone marrow pathology with different diffusion properties.

## Materials and Methods

### 1. The phantom study

A phantom study using two diffusion weighted sequences for evaluation of the diffusion coefficient was performed. Three water-containing cylinders at different temperatures were designed: phantom A was 3℃, B was 23℃, and C was 63℃. Diffusion movement of the water molecules increased as the temperature increased. The EPI-DWI is already a well-established sequence that has proved to be useful for the assessment of diffusion measurements. Both SSFP and EPI sequences were evaluated for comparison of the diffusion properties. The signal to noise ratios (SNR) and/or ADC values of the three phantoms using each diffusion-weighting sequence were assessed. The sequence parameters of the SSFP were the same as in the clinical study.

### 2. A clinical study

SSFP- DWI was performed in 28 patients [sacral insufficiency fractures (10) osteoporotic lumbar compression fractures (10) and malignant compression fractures (8)]. The sacral insufficiency fractures and the osteoporotic compression fractures were confirmed by computed tomography and/or 6 to 12 months of clinical follow up. Metastatic tumors (five breast cancers, two lung cancers, and one stomach cancer) were diagnosed by CT-guided biopsy. Spin-echo MR imaging and DWI were performed for all of the patients. On the spin-echo sequences, the axial and sagittal T1- (repetition time[TR]/ echo time[TE]: 583/12msec), turbo-T2-weighted images (3800/128msec) and contrast enhanced T1-weighted images with fat suppression sequences were obtained. The DWI sequence was based on the SSFP sequence. The sequence parameters were the following: 21.6/5/18 [TR/TE/number of excitation(NEX)]; 260mm rectangular field of view; matrix, 260×260; 6 mm slice thickness; acquisition time, 3 minutes and 6 seconds; diffusion pulse length, 2 ms. The diffusion gradient strength was 24 mT/m, with a relatively low b-value (about 165 s/mm$^2$). The diffusion gradient was applied only in the readout direction based on the previous observation that no diffusion anisotropy was found in either the phase or the section direction.[9]

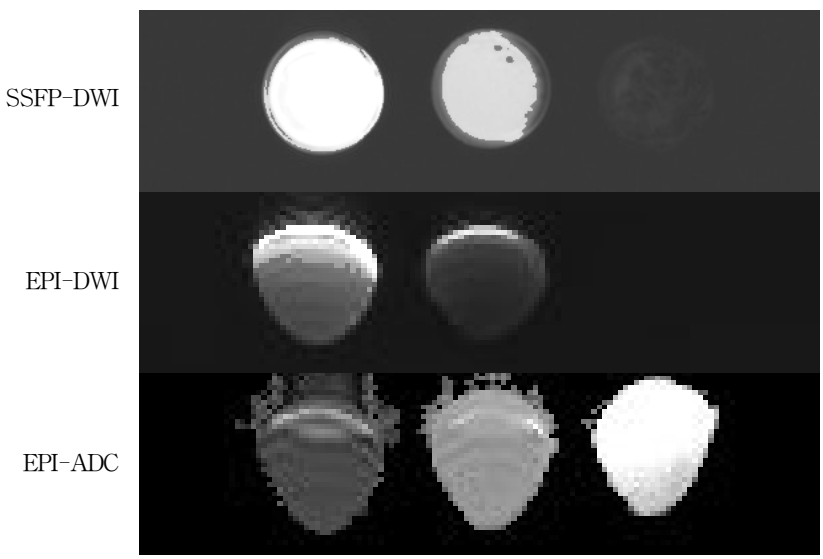
To measure the ADC maps, a diffusion-weighted single shot stimulated echo-acquisition mode sequence (650 s/mm$^2$) was obtained using the same 1.5-T MR imager. The image parameters were 1700/63/12 [TR/TE/NEX], with an 8mm slice thickness and 48×128 matrix covering a rectangular 256 mm$^2$. Whereas echo-planar imaging based diffusion measurement shows image distortion and susceptibility artifact, which is problematic in imaging of the sacrum, the single shot

Table 1. Comparison of bone marrow contrast ratios between benign and malignant fracture

| Parameter | DWI | T1-WI |
|---|---|---|
| | CR | CR |
| Benign fracture | -0.60±0.16 | -0.55±0.11 |
| Malignant fracture | 0.87±0.69 | -0.48±0.08 |

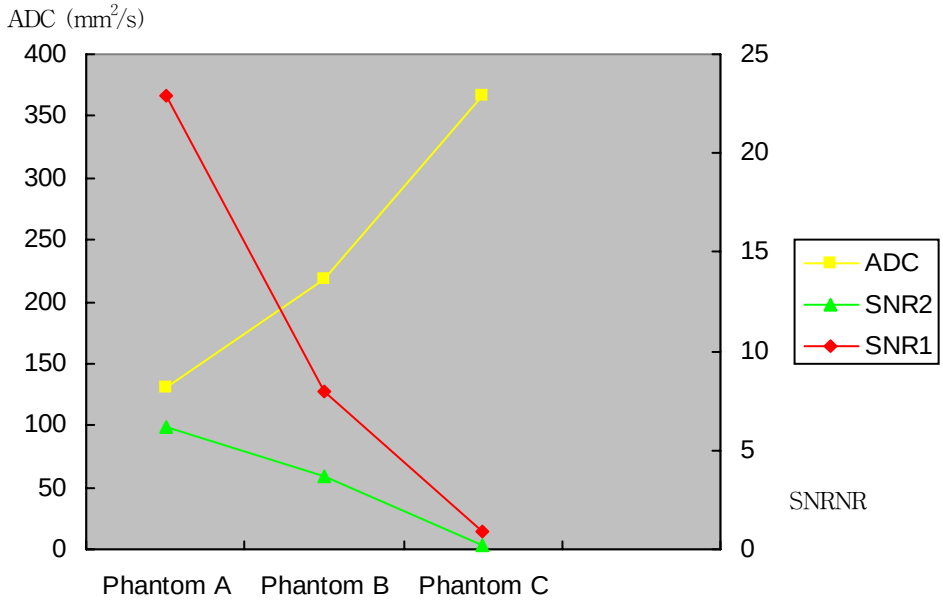
DWI, diffusion-weighted image; T1-WI, T1-weighted image; CR, contrast ratios Data are given as mean± standard deviation.

stimulated echo-acquisition mode diffusion sequence was insensitive to such problems. The ADC was calculated based on images without a diffusion gradient (b=0) and diffusion-weighted MR images (b=650s/mm$^2$). The signal intensity and contrast ratio of the benign fractures compared with the malignant fractures were evaluated. The bone marrow contrast ratios were determined as follows: $SI_A$-$SI_N$/ $SI_N$, where $SI_A$ was the signal intensity of the abnormal bone marrow and $SI_N$ was the signal intensity of the normal bone marrow. Statistical analysis of the bone marrow contrast was performed with the




ADC: Apparent diffusion coefficient
SSFP: Steady state free precession
EPI :Echo planar imaging
DWI: Diffusion-weighted image

Fig. 1. Diffusion- MR images and ADC map of phantoms using SSFP sequence and EPI based DWI. The signal intensity on SSFP as well as classic EPI-based DWI steps down as temperature increase in phantom A to C. Diffusion coefficient on ADC map is increased as temperature raise. Note geometric distortion on EPI-DWI.




SNR: Signal to noise ratio
ADC: Apparent diffusion coefficient
SSFP: Steady state free precession
EPI: Echo planar imaging

Fig. 2. SNR and ADC value of phantoms using SSFP sequence (SNR2) and EPI sequence (ADC, SNR1).

Mann-Whitney test. A p value of less than 0.01 was considered to indicate a statistically significant difference.

## Results

On the phantom study, the signal intensity on the SSFP as well as the classic EPI-based DWI decreased as the temperature increased from phantom A to C (Fig. 1). ADC values of the phantoms on EPI-DWI were $0.13\times10^{-3}$ $mm^2/s$ in phantom A, $0.22\times10^{-3}$ $mm^2/s$ in B and $0.37\times10^{-3}$ $mm^2/s$. in C (Fig. 2). The SSFP can be regarded as a DWI sequence in view of the series of signal decreases. For all of the patients with benign and malignant fractures, the spin-echo MR images showed nonspecific signal intensity such as a low signal intensity on the T1-weighted images and strong enhancement on the contrast-enhanced T1-weighted images with fat suppression. The T2-weighted images showed heterogeneous signal intensities. On the SSFP, all benign fractures were hypointense to the adjacent normal bone marrow and the malignant fractures were hyperintense (Fig 3-5). For the contrast ratios on the SSFP, the benign fractures had negative values,

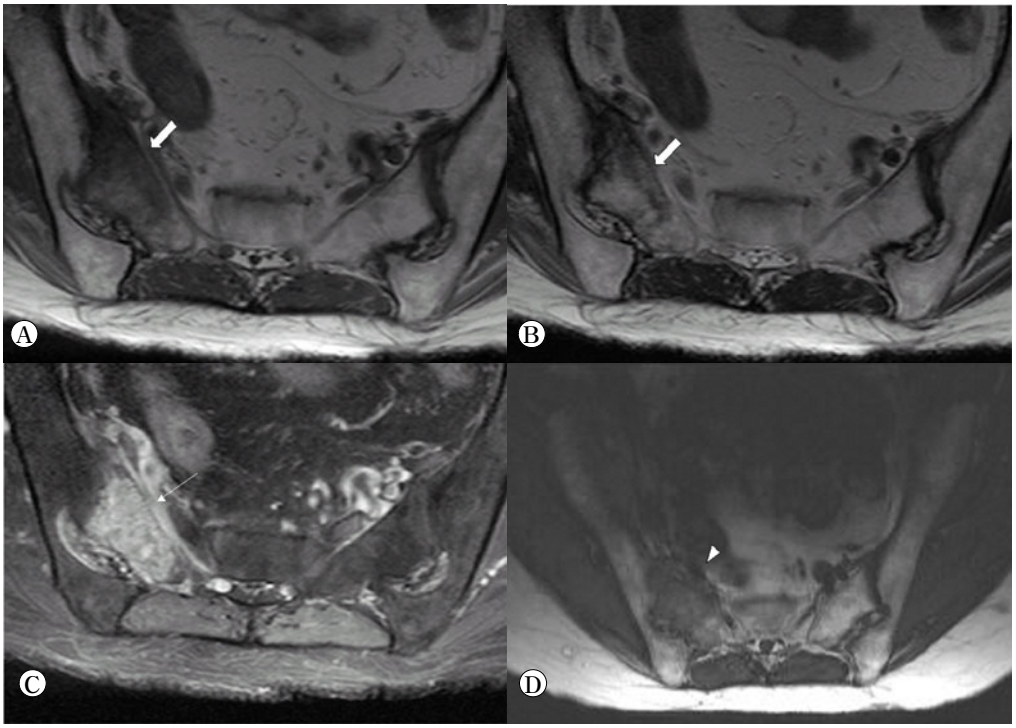



Fig. 3. Sacral insufficiency fracture (right sacral alae).

T1- (A) and T2-weighted MR images (B) demonstrate low signal intensity in the right sacral alae (thick arrow). Contrast enhanced T1-weighted MR image with fat suppression (C) shows enhancement (arrow). Diffusion-weighted MR image (D) reveals hypointense (arrowhead).

but the malignant fractures were positive ($P$<0.001) (Table 1). The mean ADC values were (0.88±0.07) × $10^{-3}$ $mm^2/s$ in sacral insufficiency fractures and (0.78±0.03) × $10^{-3}$ $mm^2/s$ for metastatic tumors of the sacrum. Normal bone marrow showed a mean ADC value of (0.21 ± 0.06) × $10^{-3}$ $mm^2/s$.

## Discussion

SSFP-DWI of the bone marrow is a new MR imaging method. Several studies have shown significantly different diffusion rates for various pathological conditions such as edema and tumors. We evaluated a phantom study to determine the diffusion of water molecules using the SSFP sequence. The signal attenuation due to diffusion in this SSFP sequence was derived and confirmed experimentally by phantoms; hot water with increased movement of the water molecules resulted in a hypointense signal compared to cold or lukewarm water with relatively decreased movement of water molecules. Our phantom study with SSFP imaging showed a similar result as that of the EPI based DWI. SSFP - DWI with a low b- value was a reliable imaging sequence to evaluate the

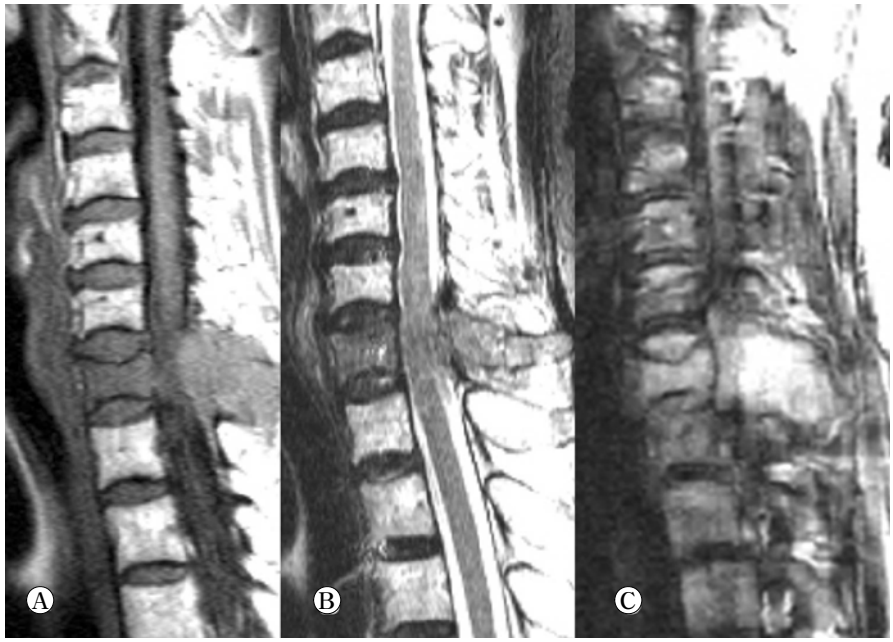



Fig. 4. Metastatic compression fracture of C7 in breast carcinoma.

T1 (A) and T2 (B) -weighted images show compression fracture with low signal intensity at C7. Hyperintensity at same location on SSFP-DWI (C) is noted.

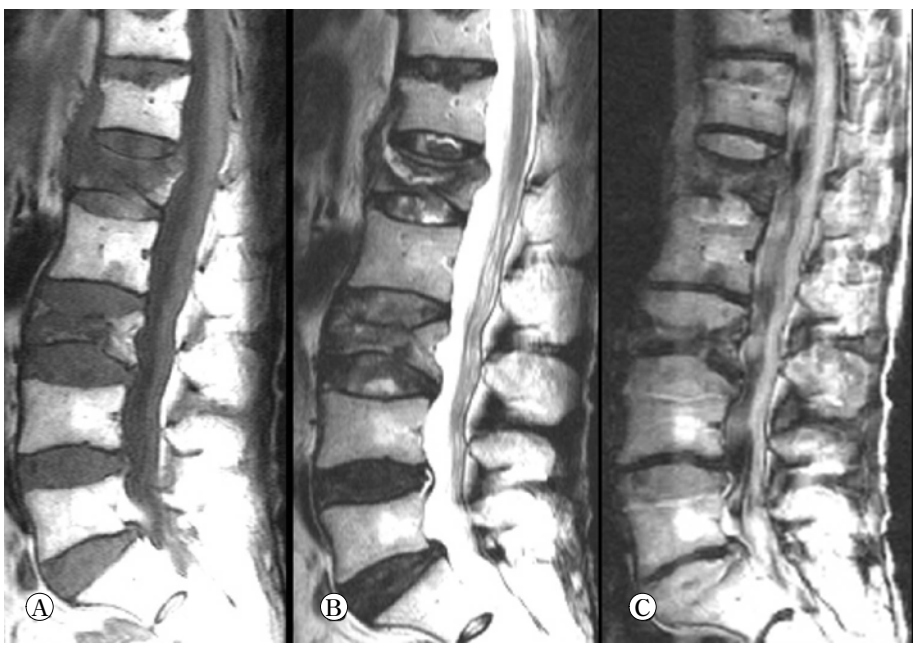



Fig. 5. Benign compression fractures at L1 and L3 bodies.

TT1 (A) and T2 (B) -weighted images show compression fracture with low signal intensity at L1 and L3 bodies. SSFP-DWI (C) shows low signal intensity at the same locations.

diffusion measurements of bone marrow pathology. The EPI-DWI with high b-value cannot be used for bone marrow pathology due to the high susceptibility to artifact.

There are several reports on SSFP-DWI used to diagnose spinal bone marrow disease.[9-11] Baur et al reported that SSFP-DWI in the vertebral bone marrow provided excellent differentiation between malignant and benign compression fractures. They reported that all the pathological vertebral compression fractures were hyperintense to the adjacent normal vertebral bodies, but all of the benign compression fractures were hypo- to isointense. A possible explanation for their results was that for malignant fractures, the reduction of the extracellular volume in the densely packed tumor tissue might lead to a decrease in the ADC, resulting in an increase in the signal intensity.[9]

In the current study, osteoporosis induced benign compression fractures and non-compression sacral insufficiency fractures were hypointense on the SSFP- DWI. A possible explanation for the hypointense benign fractures on the DWI is the increase of free water in the bone marrow caused by edema that leads to an increased extracellular volume fraction. Therefore, the ADC is high, which produces a low signal intensity for the benign fractures on the DWI. By contrast, tumors are associated with narrow interstitial spaces that may cause a decrease ADC and result in a hyperintense signal.

In our study although the cases evaluated for ADC values were small, the ADC map of the benign fractures showed a greater increased in diffusion than did the malignant fractures. Published studies have reported the calculations for the ADC values with diffusion-weighted single shot sequences. They reported different ADC values for benign spinal compression fractures and metastases with variable ranges of b-values. Chan et al.[10] used a single-shot echo planar sequence. They measured four b-values ranging from 200 to 1000 s/mm$^2$. The mean ADC values were $1.94\times10^{-3}$ mm$^2$/s for benign compression fractures and $0.82\times10^{-3}$ mm$^2$/s for neoplastic vertebral compression fractures. Zhou et al.[11] used a single-shot fast-SE sequence with b values ranging from 0 to 250 s/mm$^2$. The ADC values were $0.32\times10^{-3}$ for benign fractures and $0.19\times10^{-3}$ mm$^2$/s for metastatic fractures. The differences for the ADC values of benign fracture and metastatic fractures, reported in the study by Chan et al.,[10] might be explained by the fact that the maximum diffusion-weighted sequences was significantly different, as were the sequences.

In conclusion, bone marrow pathology with different diffusion coefficients was evaluated by SSFP-DWI. All benign fractures were hypointense to the adjacent normal bone marrow and the malignant fractures were hyperintense.

## Summary

The signal intensity changes in water phantoms, with different diffusion coefficients on SSFP (low b-value) as well as EPI-DWI (high b-value) were measured. Bone marrow pathology with different diffusion coefficients was evaluated by SSFP-DWI. On the SSFP, all benign fractures were hypointense compared to the adjacent normal bone marrow and the malignant fractures were hyperintense.

## 요 약

### 목 적

이 연구는 낮은 b값의 SSFP-확산강조영상에 의한 물분자의 확산 성질 측정이 가능한지를 알기 위한 모형연구를 하고 이 기법이 골수질환에 적용이 가능한 가를 아는 것이 목적이다.

### 재료 및 방법

모형 연구 : 순수한 물로 구성된 모형에서 확산강조 영상을 시행하였다. 섭씨 3도, 23도 그리고 63도의 순수한 물로 구성된 모형에서 SSFP 확산강조영상과 echo plannar imaging (EPI) 확산강조영상 (b값: 1000 s/mm$^2$)을 모두 시행하여 각각에서 신호 대 잡음 비 (SNR; signal to noise ratio)와 확산계수를 얻었다.

임상 연구 : 10명의 천골 부족 골절, 10명의 골다공증에 의한 급성 요추 압박골절, 그리고 전이암에 의한 요추 압박골절 8명에서 각각 SSFP 확산강조영상을 시행하였다. SSFP 확산강조영상 외 확산계수를 측정하기 위해 single shot stimulated echo-acquisition mode sequence를 이용한 확산강조영상을 시행하였다.

### 결 과

모형연구에서 EPI 확산 강조영상뿐만 아니라 SSFP 확산강조영상에서 물의 온도가 증가됨에 따라 신호강도의 감소를 보였다. EPI-확산계수 영상에서 확산계수 값은 3도의 물은 $0.13\times10^{-3}$ mm$^2$/s, 23도는 $0.22\times10^{-3}$ mm$^2$/s 그리고 63도에서 $0.37\times10^{-3}$ mm$^2$/s를 나타냈다. 이러한 결과는 SSFP 기법은 비록 낮은 b 값을 가지지만 확산 강조 영상으로 확신된다. SSFP 확산강조영상에서 모든 천골 부족 골절과 골다공증 척추 압박골절은 높은 확산계수를 의미하는 저신호강도를 전이암에 의한 압박골절은 낮은 확산 값을 나타내는 고신호 강도를 보였다.

### 결 론

SSFP 확산강조영상에서 다른 확산계수를 가진 골수질환이 영상화 되었으며 모든 양성골절은 주위 정상 골수에 비해 저신호강도, 악성종양에 의한 골절은 고신호강도로 관찰되었다.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