

# Vertebral Body Compression Fracture: Discriminating Benign from Malignant Causes by Diffusion-Weighted MR Imaging and Apparent Diffusion Coefficient Value

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**Objective:** To evaluate the diagnostic performance of apparent diffusion coefficient (ADC) value in discriminating benign from malignant vertebral compression fracture.

**Material and Method:** 22 symptomatic patients with compression fracture of vertebra referred for conventional MRI spines during January 2009-March 2010 underwent additional diffusion weighted MR techniques. Evaluation of diffusion weighted MR imaging and quantified ADC value from reconstructed ADC map were performed. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of apparent diffusion coefficient (ADC) value were calculated.

**Results:** A total of 39 vertebral fractures; 7 malignant compression fractures and 32 benign compression fractures were evaluated. The difference between ADC values of malignant, benign compression fracture and normal vertebrae were statistically significant ( $p < 0.0001$ ). The accuracy, sensitivity and specificity were 89.7%, 85.7% and 90.6% respectively with the ADC threshold of 0.89 to discriminate malignancy.

**Conclusion:** The ADC promises to be an effective implement for characterization of vertebral body compression fracture in differentiating benign and malignant compression fractures.

**Keywords:** Vertebral body, Compression fracture, Diffusion weighted, ADC value

*J Med Assoc Thai* 2012; 95 (1): 81-7

Full text. e-Journal: <http://www.jmat.mat.or.th>

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Vertebral compression fracture is one of the most common clinical problems in the elderly. Magnetic resonance (MR) imaging has been applied to discriminate benign and malignant vertebral body collapse. Many findings have been described, such as convex posterior border of the vertebral body, abnormal signal intensity of the pedicle or the posterior element, epidural mass or visualized fracture line<sup>(1-4)</sup>. However, using these findings for differentiating between benign and malignant vertebral fractures may sometimes be difficult.

Diffusion weighted MR imaging (DWI) is a technique which has been used for many years in neuroradiology. DWI is sensitive for movement of water molecules in intracellular and extracellular

compartments. This fact can be used for tissue characterization<sup>(5)</sup>. In cellular tissue, there is restriction of water molecular movement, resulting in lower phase shifting and lower signal attenuation<sup>(6)</sup>. Baur et al reported their preliminary results using DWI in differentiation between benign and malignant acute vertebral compression fracture<sup>(7)</sup>. They concluded that DWI provided excellent distinction between pathologic and benign vertebral compression fractures. Their result was similar to the other study<sup>(8)</sup>. However, Castillo et al found that DWI offered no advantage over routine noncontrast MR imaging in the detection of vertebral metastases<sup>(9)</sup>.

Due to this controversy, other investigators have used DWI techniques that allowed for the calculation of apparent diffusion coefficient (ADC) values<sup>(8,10,11)</sup>. Quantitative evaluation was proved to demonstrate a statistically significant differentiation between benign and malignant compression fracture.

In the authors' Siriraj Hospital, collapsed vertebra in the elderly is often a diagnostic problem

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when controversy of conventional MR images is present in differentiating benign conditions from tumor. The purpose of the present study was to evaluate the usefulness of DWI and quantitative ADC value in discriminating benign and malignant compression fractures.

### Material and Method

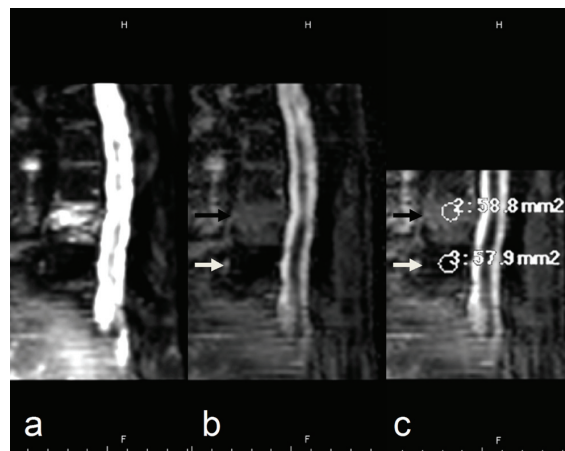
The present prospective study was performed during January 2009 to March 2010 in 22 symptomatic patients with collapsed vertebral body who were referred for MRI of the spines. Inclusion criteria of the patients were age more than 35 years old and conventional MR images showing collapsed vertebral body.

All MR images were performed with a 3.0T MRI scanner (Archieva, Philips, Best, the Netherlands). The scanning sequence were as follows; sagittal T1W spin echo (repetition time msec/echo time msec = 450/12), sagittal T2W spin echo and axial T2W spin echo (repetition time msec/echo time msec = 120/3,000) and sagittal STIR spine echo (repetition time msec/echo time msec = 3,500/80). In addition, T1W with fat saturation in sagittal and axial planes were obtained after intravenous administration of 0.1 mmol/kg gadolinium contrast media in 6 cases.

The MR pulse sequence used for DWI was a single shot echo planar pulse sequence with the following imaging parameters: axial plane, TR 7,000 msec, TE 55 msec, receiver bandwidth 17 kHz, field of view 224 cm x 224 cm, matrix size 112 x 112, slice thickness 2 mm, interslice gap 0 mm, b-value 0 and 400 s mm<sup>-2</sup> and fat suppression (SPIR). The images were performed before gadolinium injection at the suspected collapsed vertebral bodies. Sagittal reformation was performed from the axial data.

The signal intensities of corresponding T1W images, T2W images, STIR images and DWI (with b = 400 s mm<sup>-2</sup>) were evaluated and compared. The sagittal T1W, T2W, STIR and DWI were analyzed by two radiologists who were blind from clinical information. The following findings were assessed; (1) abnormal bone marrow signal intensity (2) convex of posterior border of the vertebral body (3) paravertebral soft tissue mass and (4) involvement of posterior element on MR imagings. The final decision was made by consensus.

The apparent diffusion coefficient (ADC) map was reconstructed on commercial work station (View Forum, Philips). Quantitative ADC value was measured by placing a region of interest (ROI) cursor



**Fig. 1** 84-year-old man with compression fracture due to osteoporosis. (a) Sagittal DWI showing hyper-signal intensity at collapsed vertebra. (b, c) Sagittal ADC map showing location of region of interest (ROI) cursor in the fracture thoracic vertebral body (black arrow) and normal vertebral body (white arrow)

at the center of abnormal vertebral bodies with homogeneous signal intensity on the ADC map (Fig. 1). In vertebral bodies with inhomogeneous signal intensities, the ROI was placed at corresponding area of enhancement which seen on sagittal post contrast images. In addition the ADC value of normal vertebral bodies above or below the abnormal vertebral bodies were measured in all cases by placing ROI at the center of the vertebral bodies.

The pathological result was used as the gold standard. In patients without pathological proven, conclusion from clinical information and follow-up imaging were used for the final diagnosis.

The statistical analysis was performed to compare ADC values of normal vertebral bodies, benign and malignant compression fractures by using the Student's t-test. A p-value of less than 0.05 was considered statistical significant difference.

The present study was approved by Siriraj institutional ethical review board (COA no. Si 551/2008).

### Results

A total of 39 vertebral body collapse were found in 22 patients: 12 patients with single level lesion and 10 patients with multiple levels of lesions. There were 8 men and 14 women with range of age of 35-84 years old; mean age 54.63 years old. Biopsy was performed in 2 patients (uterine cervical cancer and

hepatocellular carcinoma). Biopsy was not performed in 19 patients because of apparent history of trauma, no known history of malignancy and the absence of convex of posterior border of vertebral body, paravertebral soft tissue mass and involvement of posterior element on conventional MR imagings. Of 1 patient with underlying lung cancer, the biopsy was not performed due to severe clinical illness of the patient. The diagnosis was made under clinical and imaging information.

Among 39 vertebral fractures, 10 lesions (25.6%) were found in the cervical spines, 4 lesions (10.3%) in the thoracic spines and 25 lesions (64.1%) in the lumbar spines. Of these vertebral lesions were classified as malignant in 7 and benign in 32 vertebral fractures. These 39 lesions showed heterogeneity in signal intensity on T1W, T2W, STIR and DWI (Table 1).

Three patients in the malignant group were all women with mean age 45.33 years olds. The primary malignancy was hepatocellular carcinoma, cervical carcinoma and lung cancer. Biopsy in the patient with uterine cervical cancer showed pathologically to be squamous cell carcinoma, moderate differentiation. In the hepatocellular carcinoma patient, the result from laminectomy was negative for malignancy. However, this patient was diagnosed with vertebral

metastasis by clinical informations, bone scintigraphy and MR imaging of the spines which were typical for malignancy.

All of the malignant vertebral body compression fractures (n = 7), were hypointense on T1W images, hyperintense on T2W images and STIR images and hyperintense on DWI (Fig. 2) with respect to normal bone marrow. All lesions were associated with posterior element involvement, 6 lesions were associated with epidural mass and 4 lesions were associated with convex posterior border of the vertebral body.

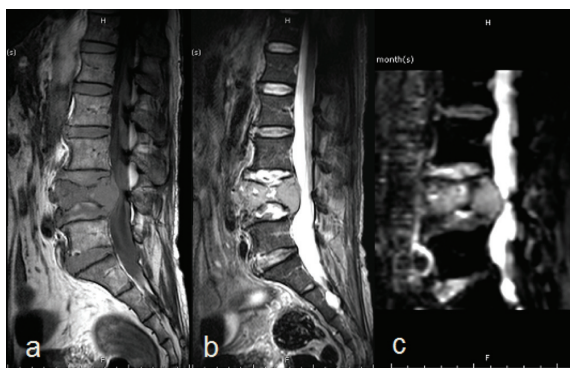
Thirty-two benign vertebral fractures including 23 osteoporotic compression fractures, 4 traumatic fractures and 5 infections. In 5 vertebral infections, 3 lesions were found in a case of tuberculous spondylitis and 2 lesions in a case of bacterial osteomyelitis. Final diagnosis of these benign lesions were concluded from clinical and other follow-up imaging findings.

The signal intensity of benign lesions were hypointense in 22 lesions (68.8%), isointense in 4 lesions (12.5%), hyperintense in 1 lesion (3.1%) and mixed signal intensities (hyperintense and hypointense) in 5 lesions (15.6%) with respect to normal bone marrow on T1W images. On T2W images, there were hyperintense in 16 lesions (50.0%),

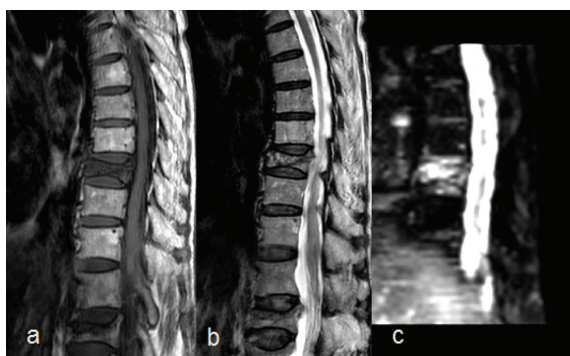
**Table 1.** Signal intensity of malignant and benign vertebral compression fractures on T1W, T2W, STIR and DW images

MRI Findings	Malignant vertebral fractures (n = 7)	Benign vertebral fractures (n = 32)
Signal intensity of vertebral body on T1W image		
Hypo SI	7 (100%)	22 (68.8%)
Iso SI	0	4 (12.5%)
Hyper SI	0	1 (3.1%)
Mixed SI	0	5 (15.6%)
Signal intensity of vertebral body on T2W image		
Hypo SI	0	0
Iso SI	0	4 (12.5%)
Hyper SI	7 (100%)	16 (50%)
Mixed SI	0	12 (37.5%)
Signal intensity of vertebral body on STIR image		
Hypo SI	0	0
Iso SI	0	2 (9.1%)
Hyper SI	7 (100%)	13 (59.1%)
Mixed SI	0	7 (31.8%)
Signal intensity of vertebral body on DW image		
Hypo or iso SI	0	19 (59.4%)
Hyper SI	7 (100%)	13 (40.6%)

\* SI = signal intensity



**Fig. 2** Malignant vertebral compression fracture. (a, b, c) MR images of lumbar spines of a 60-year-old woman with a history of hepatocellular carcinoma who presented with back pain. (a) Pre-Gadolinium T1-weighted image in sagittal plane showing hypointensity (b) STIR MR image in sagittal plane showing hypersignal intensity (c) Sagittal MR DW image with b-factor of 400 s mm<sup>2</sup> showing hypersignal intensity with respect to normal bone marrow



**Fig. 3** Benign compression fracture (a, b, c) MR images of the thoracic spines in a 84-year-old man who presented with paraplegia. (a) Pre-Gadolinium T1-weighted image in sagittal plain showing hypointensity at T9 vertebra. (b) T2-weighted image in sagittal plain showing mixed intensity and (c) Sagittal DWI with b-factor of 400 s mm<sup>2</sup> showing hypersignal intensity with respect to normal bone marrow

isointense in 4 lesions (12.5%) and mixed signal intensities in 12 lesions (37.5%) with respect to normal bone marrow. In 15 patients with STIR images, there was hyperintense in 13 lesions (59.1%), isointense in 2 lesions (9.1%) and mixed signal intensities in 7 lesions (31.8%) with respect to normal bone marrow. DWI were hyperintense in 13 lesions (40.6%) and

hypointense in 19 lesions (59.4%) with respect to normal bone marrow (Table 1, Fig. 3).

The mean ADC values were  $(0.24 \pm 0.09) \times 10^{-3} \text{ mm}^2 \text{ sec}^{-1}$  in normal vertebral bodies,  $(0.75 \pm 0.13) \times 10^{-3} \text{ mm}^2 \text{ sec}^{-1}$  in malignant vertebral body compression fractures and  $(1.44 \pm 0.50) \times 10^{-3} \text{ mm}^2 \text{ sec}^{-1}$  in benign vertebral body compression fractures. The ADC value of the malignant vertebral lesions were statistically significant higher than those of the normal vertebral bodies ( $p < 0.0001$ , 95% CI = 0.43-0.59) and lower than those of benign vertebral lesions ( $p < 0.0001$ , 95% CI = 0.87-1.01). These data was summarized in Table 2.

When the threshold points of ADC value greater than or equal to 0.89 was selected for benign lesion. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 85.7% (95% CI 48.68-97.43), 90.6% (95% CI 75.78-96.76), 66.7% (95% CI 35.42-87.94), 96.7% (95% CI 83.32-99.40) and 89.7% (95% CI 73.29-94.40) respectively. At this threshold point, false positive and false negative for malignancy were 7.7% (n = 3) and 2.6% (n = 1) respectively.

## Discussion

MR imaging is a good method for evaluating the bone marrow and has been applied for several years to differentiate benign from malignant fractures<sup>(1-4,12,13)</sup>. Although application of combination of several signs is still not specific enough.

DWI is a sequence which is sensitive to the diffusion of tissue water molecule. The signal intensity of DWI depends on the degree of water movement in both intracellular and extracellular compartments. Water in viable tumor cells appears to have less mobility due to hypercellular structures<sup>(14)</sup>. In vertebral metastasis, there is infiltration of tumor cells replacing the fat cell

**Table 2.** ADC values of normal vertebral bodies, benign compression fractures and malignant compression fractures

Findings	ADC value ( $\times 10^{-3} \text{ mm}^2 \text{ sec}^{-1}$ )
Normal vertebral bodies (n = 22)	$0.24 \pm 0.09$
Malignant compression fractures (n = 7)	$0.75 \pm 0.13^*$
Benign compression fractures (n = 32)	$1.44 \pm 0.50^\#$

\* p-value < 0.0001 compared with normal vertebral body (Student's t-test)

# p-value < 0.0001 compared with malignant compression fractures (Student's t-test)



in the marrow. Packing of tumor cells result in restriction of diffusion of water molecules and provided hypersignal intensity on DWI. In benign compression fractures an increasing amount of free water content in the interstitial space due to edema or hemorrhage, leads to an increase in the extracellular volume fraction relative to adjacent normal bone marrow. Thus, the water molecule mobility in benign vertebral fracture is increased, resulting in facilitation of diffusion in that region. From this concept, the ADC value is maximized in benign vertebral fracture and minimized in normal vertebral bodies<sup>(10)</sup>.

DWI in the present study had fat suppression effect. Thus, on DW imaging, the fatty marrow signal was null. The normal vertebral body has insignificant amount of free water content in the interstitial space and only small amount of mobile protons in normal vertebral body are available, resulting in low ADC value in normal vertebral body<sup>(10)</sup>. In the present study, the mean ADC value of normal vertebral bodies was about  $(0.24 \pm 0.09) \times 10^3 \text{ mm}^2 \text{ sec}^{-1}$  which is similar to previous studies of Chan et al and Ward et al<sup>(10,15)</sup>.

The ADC value of malignant compression fractures in the present study showed statistical significance more than those of the normal vertebral bodies ( $p < 0.0001$ ), but less than those of benign vertebral body compression fractures ( $p < 0.0001$ ). The authors' result was similar to the results of several previous studies which presented diffusion restriction (lower ADC value) in malignant compression fractures<sup>(8,10,11)</sup>.

Baur et al found that all 22 benign compression fractures showed hypointense on DWI and all 17 pathological fractures showed high signal intensities on DWI<sup>(7)</sup>. They concluded that the tumor packing in pathologic compression fractures caused restriction of water diffusion and led to high signal intensity on DWI. Therefore, DWI provided excellent distinction between pathologic and benign compression fractures of the spines. There were similar results in the report of Spuentrup et al which found diffusion-weighted spin-echo offered excellent distinction between benign and malignant compression fractures<sup>(6)</sup>. However, Castillo et al found that DWI offered no advantage over routine noncontrast MR imaging in detection and characterization of vertebral metastasis. Because of malignant lesions in their study showed both hyper and hypo signal intensities<sup>(9)</sup>. In the present study, the authors also found a variable pattern of signal intensity on DWI in benign lesions.

In the present study, the ADC values of benign lesions were high about  $(0.96-2.37) \times 10^{-3} \text{ mm}^2 \text{ sec}^{-1}$ , represented no restriction. So, hyperintense signal on DWI in this group was likely due to influence of T2 shine-through effect. The other research of Baur et al reported that to make the signal intensity dependent on diffusion term (which decreased effect of T2 relaxation term), it was necessary to use sufficient large b-factor. Benign fractures became progressively hypointense, then reducing the number of false positive results<sup>(16)</sup>. Other authors have accomplished similar results by using b-values as high as 880-1,000  $\text{sec}/\text{mm}^2$ <sup>(10,11)</sup>. In the authors' study, b-value was selected at 400  $\text{sec}/\text{mm}^2$ . This was the possible cause of hyper- signal intensity in several cases of the authors' benign fractures. By using higher b-value, this problem should be corrected.

There were some limitations in the authors' study. First, there was a small number of subjects, especially of the malignant lesions. Second, there was only 1 histologic confirmation and combination of MR and clinical data was used to make the diagnosis for the majority of the patients.

## Conclusion

In summary, the ADC mapping should be reconstructed in all cases which performed DWI for eliminated effect of T2 shine-through. The T2 shine-through effect causes false positive in several benign fractures in the present study, may be due to using rather low b-value (400  $\text{sec}/\text{mm}^2$ ). The ADC promises to be an effective implement for characterization of vertebral body compression fracture, which may improve diagnostic efficacy of MR imaging in evaluation of spinal lesions.

## Potential conflicts of interest

Research division, Faculty of Medicine Siriraj Hospital.

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ความแม่นยำในการวินิจฉัยแยกภาวะกระดูกสันหลังหักจากมะเร็งลุกลามและไม่ใช้สาเหตุจากมะเร็งลุกลามโดยใช้เทคนิค *diffusion-weighted* และค่า *apparent diffusion coefficient* ของการตรวจด้วยคลื่นแม่เหล็กไฟฟ้า

สุวิมล วงศ์ลักษณะพิมล, อรสา ชวาลภาฤทธิ์, สุทธิพร คำพันธุ์นิพ, สิริอร ตริตระการ, พิพัฒน์ เขียววิทย์, พนิดา ชาญเชาว์วานิช

**วัตถุประสงค์:** เพื่อศึกษาความแม่นยำในการวินิจฉัยแยกโรคของผู้ป่วยกระดูกสันหลังหักจากภาวะมะเร็งลุกลามจากสาเหตุอื่น ๆ โดยใช้เทคนิค *diffusion-weighted* และ ค่า *apparent diffusion coefficient* ของการตรวจด้วยคลื่นแม่เหล็กไฟฟ้า

**วัสดุและวิธีการ:** ศึกษาจากผู้ป่วย 22 ราย ที่มารับการตรวจคลื่นแม่เหล็กไฟฟ้าของกระดูกสันหลังแล้วพบภาวะกระดูกสันหลังหัก แบบยุบตัวตั้งแต่เดือนมกราคม พ.ศ. 2552 ถึง มีนาคม พ.ศ. 2553 ซึ่งจะได้รับการตรวจเพิ่มเติมด้วยเทคนิค *diffusion-weighted* และคำนวณหาค่า *apparent diffusion coefficient* เพื่อการศึกษาความไว, ความจำเพาะ และความแม่นยำ

**ผลการศึกษา:** จากกระดูกสันหลังหักแบบยุบตัวทั้งหมด 39 รอยโรค ซึ่งแบ่งเป็นกระดูกสันหลังยุบตัวจากมะเร็งลุกลาม 7 รอยโรค และกระดูกสันหลังยุบตัวจากสาเหตุอื่นที่ไม่ใช่มะเร็งลุกลาม 32 รอยโรค จากการคำนวณค่า *apparent diffusion coefficient* พบว่ามีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างกระดูกสันหลังปกติ, กระดูกสันหลังยุบตัวจากมะเร็งลุกลามและกระดูกสันหลังยุบตัวจากสาเหตุอื่นที่ไม่ใช่มะเร็งลุกลาม ประเมินความแม่นยำ, ความจำเพาะ และความไวได้ 89.7%, 85.7% และ 90.6% ตามลำดับ

**สรุป:** ค่า *apparent diffusion coefficient* จากการตรวจด้วยคลื่นแม่เหล็กไฟฟ้าน่าจะเป็นเทคนิคที่ช่วยเพิ่มความแม่นยำในการวินิจฉัยแยกโรคของผู้ป่วยกระดูกสันหลังหัก จากภาวะมะเร็งลุกลามจากสาเหตุอื่นที่ไม่ใช่มะเร็งลุกลาม

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