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*Original Article*

# Percutaneous vertebral puncture biopsy and MRI are useful in diagnosis of malignant vertebral fractures

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**Abstract:** This study is to investigate the clinical application of percutaneous vertebral puncture biopsy and MRI in diagnosis of malignant vertebral fractures. A total of 46 patients were enrolled in this study. Percutaneous kyphoplasty was performed for each patient. The coaxial puncture biopsies in broken spines were conducted. The pathological results were compared with the magnetic resonance imaging (MRI) results. The MRI scan showed that there were 67 possible malignant vertebral fractures in 46 patients. Among the 67 possible malignant vertebral fractures, 64 were successfully confirmed by pathological examination. The successfulness and positive rates in biopsy were 95.52% and 76.56%, respectively. No complication occurred. Kappa analysis indicated that preoperative MRI for malignant vertebral fracture was consistent with biopsy. Percutaneous vertebral puncture biopsy and MRI are useful in diagnosis of malignant vertebral fractures.

**Keywords:** Vertebral fractures, malignant, magnetic resonance imaging

## Introduction

The incidence of tumors is increasing in recent years. Approximately 40-80% of tumor patients suffer from spinal metastases. Early and appropriate diagnosis and proper treatments increase the therapeutic effects, improving quality of life of the patients. Magnetic resonance imaging (MRI), diffusion-weighted imaging (DWI), and PET/CT facilitate the preoperative diagnosis of malignant vertebral fractures [1-14]. Evidence obtained from MRI is helpful for preliminary etiologic diagnosis of benign and malignant vertebral fractures [1, 12, 15]. Evidence reflecting malignant vertebral fractures in MRI images include soft tissue mass surrounding vertebral, low T1 uniform signal, posterior margin spherical convex to the spinal canal, pedicle involvement, and multi vertebral skipping involvement. However, this information cannot be used as specific marker for malignant fractures, since they are varying in accuracy, specificity, and sensitivity. Similarly, PET/CT scan cannot provide necessary information for pathological diagnosis. Currently, pathological examination has been considered as the most accurate diagnostic method for fractures, since pathological examination can determine the nature of factures and histological origin and differentiation of malignancies. There were many risks in incision or excision biopsy due to the complex structures and deep localization of the tissues surrounding the spinal. Through percutaneous vertebral puncture biopsy, some vertebral lesions for pathological examination may be obtained via working channel, thereby determining the etiology and primary diseases of vertebral fractures, and providing evidence for subsequent clinical treatments [16-19].

In this study, we evaluated patients who underwent percutaneous kyphoplasty (PKP) in our hospital for curing of vertebral compression fractures. MRI scan was performed for all patients before surgery. While performing PKP, we conducted coaxial puncture biopsy for 46 patients who may have malignant vertebral fractures.

## Materials and methods

### *Information of patients*

In this study, 67 vertebral biopsies in 46 patients (25 males and 21 females) (37 to 84 years;

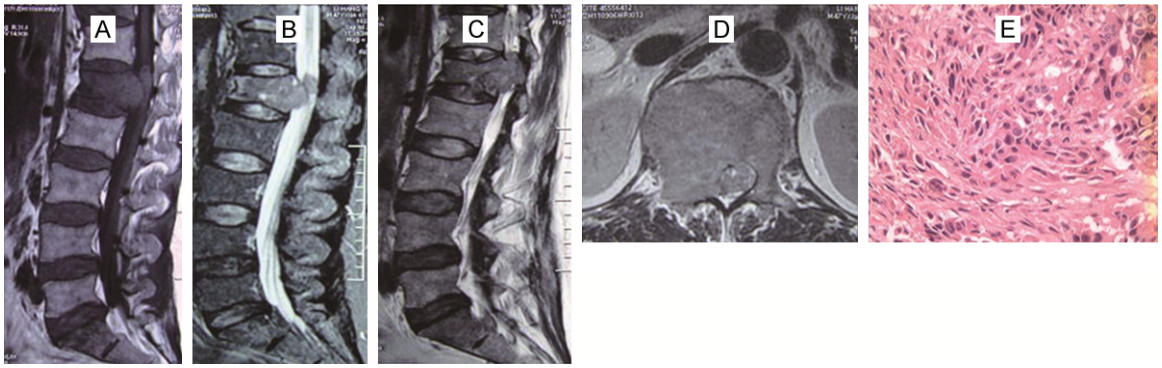


**Figure 1.** Case 1, male, 47-year old. The preoperative MRI showed low T1 uniform signal, posterior margin spherical bulge, epidural mass, and right pedicle involvement. Pathological fractures due to metastatic lung cancer were determined by biopsy. A. Low T1 uniform signal; B. High T2WI signal; C. High STIR signal; D. Plane; E. Pathology examination indicated that this is an adenocarcinoma. The immunohistochemical markers were consistent with adenocarcinoma with a lung origin. Immunohistochemical staining showed: TTF-1(+), CK7(+), CK20(-), Villin(-), CK5/6(-).

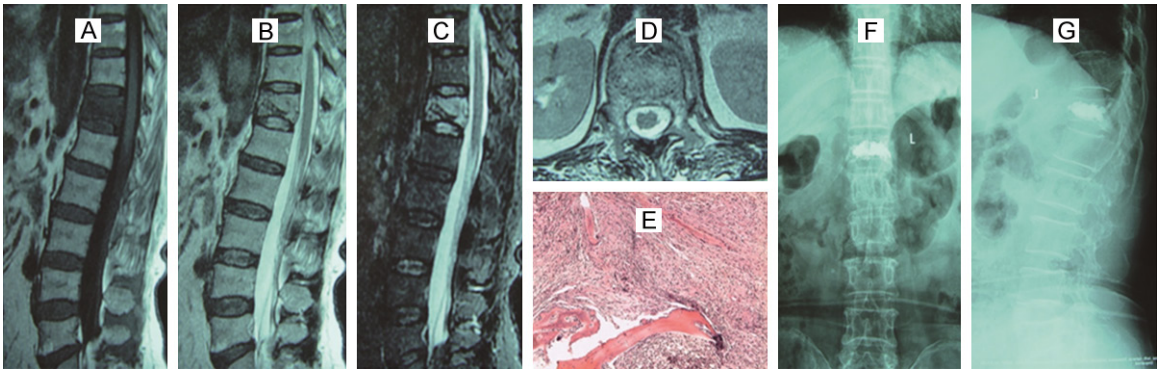


**Figure 2.** Case 2, female, 66-year old. The preoperative MRI showed low T1 uniform signal, posterior margin spherical bulge, and unexlusive malignant T12 vertebral compression fractures. Benign fractures were determined by biopsy and PKP was performed. A. Low T1 uniform signal; B. High T2WI signal; C. High STIR signal; D. Plane; E. Abundant fibrous tissue hyperplasia and acute and chronic inflammatory cell infiltration among fragmental bone tissues, with more fibrin exudation; F. PA X-ray after PKP; G. LATX-ray after PKP.

mean age, 63.4 years) were performed. Prior to surgery, 23 malignancies outside spinal were determined. The study was approved by the Ethics Review Board of Shandong University. Prior written and informed consent was obtained from every patient.

The inclusion criteria included: (1) patients felt serious lower back pain, difficult to sit, stand and walk; (2) deep tenderness and percussion pain in spinous process of painful sites; (3) manifestations in MRI images such as mild kyphosis in local vertebral lesion; wedge, flat collapse or dual concave changes in broken vertebral with posterior margin spherical convex to the spinal canal; pedicle involvement; soft tissue mass surrounding vertebral; low T1 uniform signal; high or low T2WI and STIR signal (**Figures 1**, **2**); and (4) location in image was consist with tenderness and percussion pain.

The exclusion criteria were: (1) no vertebral compression fractures; (2) spinal cord or nerve compression due to posterior vertebral wall involvement; (3) bilateral pedicle destruction; (4) severe organ dysfunction, coagulopathy, or intolerance to surgery.

*Equipment*

GE XRD-DR X-ray, GE Lightspeed QX/i 16CT, GE Sigma MR/i TM 1.5 TMRI, and GE LC plus/DLX DSA were purchased from U.S. GE Company, Waukesha, Wisconsin. Vertebroplasty surgery kits were purchased from Shandong Guanlong Medical Utensils Co. LTD, Jinan, Shandong.

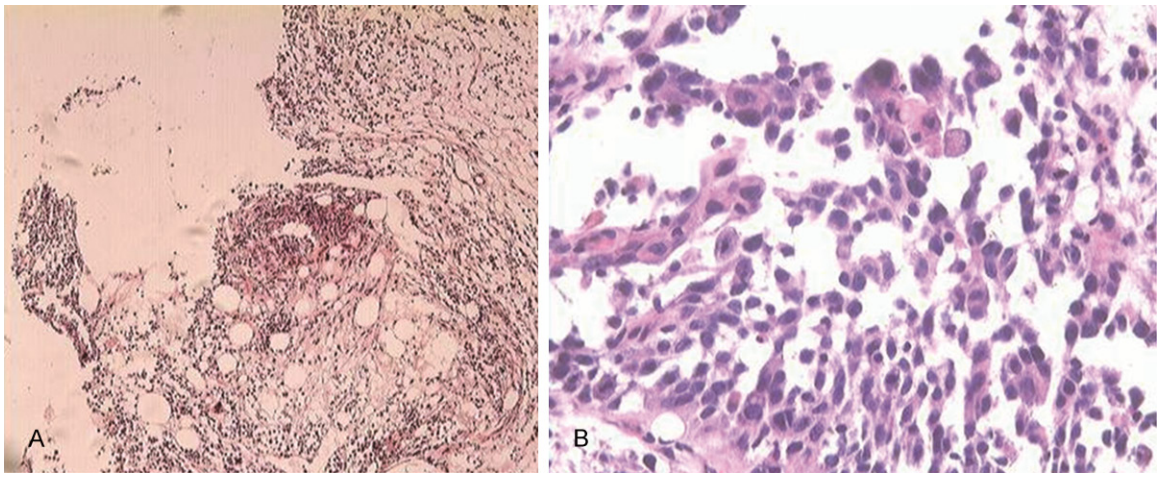


**Figure 3.** A. Case 3, male, 66-year old. MRI showed suspected malignant L1 vertebral fractures. Fibrous granulation tissue and benign vertebral fracture were detected. B. Case 4, male, 47-year old. He had a history of esophageal squamous cell carcinoma. Preoperative MRI showed malignant T12 and L1 vertebral fractures. Immunohistochemical analysis of the squamous cell carcinoma, with unknown histological origin.

**Table 1.** Clinical and pathological characteristics of patients with tumor outside spinal history

| Primary tumor | Cases | Vertebral for biopsy | Metastasis | Osteoporosis |
|---|---|---|---|---|
| Gastrointestinal | 3 | 5 | 3 | 2 |
| Lung | 7 | 8 | 6 | 2 |
| Liver | 2 | 2 | 2 | 0 |
| Breast | 6 | 9 | 7 | 2 |
| Uterine | 2 | 2 | 2 | 0 |
| Prostate | 1 | 1 | 0 | 1 |
| Larynx | 1 | 2 | 2* | 0 |
| Renal | 1 | 2 | 2 | 0 |

Note: *Cases pathologically reported to lung cancer after surgery.

**Table 2.** Clinical and pathological characteristics of patients without tumor outside spinal history

| Cases | Vertebral specimens for biopsy | Metastasis | Myeloma | Osteoporosis |
|---|---|---|---|---|
| 23* | 33# | 14* (22#) | 3* (3#) | 6* (8#) |

Note: *, Numbers of case; #, Numbers of vertebral specimens for biopsy.

**Table 3.** Evaluation of malignant vertebral fractures by the MRI and biopsy

| | +Biopsy | -Biopsy | Total | Ratio (%) |
|---|---|---|---|---|
| +MRI | 46 | 7 | 53 | 82.81 |
| -MRI | 3 | 8 | 11 | 17.19 |
| Total | 49 | 15 | 64 | |
| Ratio (%) | 76.56 | 23.44 | | |

Note: +, positive. -, negative.

*Biopsy procedure and PKP*

Patients were placed in a prone position. The digital subtraction angiography (DSA) examination was carried out to confirm the vertebral lesions. Lidocaine (1.0%) was injected around puncture point to maintain local anesthesia. Under monitoring by DSA, needle with trocar was transpedicularly punctured into spine along with direction of lesion. The needle was pulled out to establish a working channel until the tip reached the inner and posterior edge of the pedicle. The biopsy needle was inserted into spine via the working channel, reaching to 1/3 to 1/4 of the anterior-middle junction. In this way, specimen was obtained and subjected to pathological examination after fixation with 10% formalin. PKP was then performed following the standard procedure.

*Immunohistochemistry*

Paraffin sections were de-waxed and re-hydrated through an alcohol series. The endogenous peroxidase was removed, and the sections were treated with citrate buffer (0.01 M, Ph 6.0). The primary antibodies were added to the sample (50 μl), followed by incubation overnight at 4°C. The primary antibodies against

**Table 4.** The diagnostic value of biopsy for malignant vertebral compression fractures

| Biopsy characteristics | Groups | | Sensitivity (%) | Specificity (%) | Accuracy (%) |
|---|---|---|---|---|---|
| | Malignant | Benign | | | |
| Primary tumor | 39/64 | 13/64 | 86.35 | 80.87 | 83.54 |
| Metastatic tumor | 13/64 | 0/64 | 92.58 | 80.36 | 86.11 |
| Inflammation | 0/64 | 2/64 | 72.54 | 67.24 | 69.58 |

TTF-1, CK7, CK20, Villin, or CK5/6 were purchased from Anbiping Biological Company, Guangzhou, China. Then secondary antibodies were added to incubate the sections. After staining with DAB chromogenic reagent (ZSGB-BIO, Beijing, China) and counterstaining with hematoxylin for 2 min, these sections were sealed and then visualized under microscopy with the CM-2000B biomedicine image analysis system (Beihang, Beijing, China). Brown staining was considered positive. Five fields were randomly selected under high magnification (×400). The averaged number of positive cells was counted.

*Effect evaluation*

The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of MRI in diagnose of malignant vertebral fractures were calculated by comparing MRI with pathological diagnosis [5]. Sensitivity = positive MRI fractures among malignant vertebral fractures confirmed by biopsy/all fractures with malignant vertebral fractures confirmed by biopsy*100%. Specificity = negative MRI fractures among benign vertebral fractures confirmed by biopsy/all fractures with benign diseases confirmed by biopsy*100%. Accuracy = (positive MRI fractures among malignant vertebral fractures confirmed by biopsy + negative MRI fractures among benign vertebral fractures confirmed by biopsy)/all fractures participated in biopsy*100%. Positive predictive value = positive MRI fractures among malignant vertebral fractures confirmed by biopsy/(positive MRI fractures among malignant vertebral fractures confirmed by biopsy + positive MRI fractures among benign vertebral fractures confirmed by biopsy)*100%. Negative predictive value = negative MRI fractures among malignant vertebral fractures confirmed by biopsy/(negative MRI fractures among malignant vertebral fractures confirmed by biopsy + negative MRI fractures among benign vertebral fractures confirmed by biopsy)*100% [20].

*Statistical analysis*

All data was analyzed using the SPSS version 13.0 (Chicago, IL, USA). The comparative analysis between preoperative MRI and puncture biopsy in the diagnosis of malignant vertebral fractures was performed by Kappa test. ROC curve was plotted.

## Results

In 67 biopsies of malignant vertebral fractures, 64 vertebral biopsies were determined and then confirmed by pathological diagnosis, with a biopsy rate of 95.52%. The duration of biopsy for each vertebral lesion was about 3 to 15 min. There were minimal blood losses and no nerves, blood vessels or internal organ injuries during surgery. All patients had primary healing without serious complications such as pneumothorax, hemothorax, neurological dysfunction, infection and hematoma in biopsy sites.

In the 64 vertebral biopsies, there were 15 benign pathological tissues and 49 malignancies, with a positive rate of 76.56%. Benign diseases were diagnosed as osteoporotic vertebral fractures, with pathological manifestations such as fragmental bone tissues, fibrous granulation tissues (**Figures 2**, **3A**), newly bone trabecular tissues, and acute and chronic inflammatory cell infiltration. There were 16 lung cancers (**Figure 1**), 11 gastrointestinal cancers, 7 breast cancers, 4 renal carcinomas, 3 myelomas, 2 liver cancers, 2 uterine cancers, 2 poorly differentiated adenocarcinomas with unknown primary lesion and 2 squamous cell carcinomas (**Figure 3B**) in malignant fractures. In 23 patients with tumor history, tumor cells were seen in 24 specimens from 18 patients, in which, one patient with laryngeal cancer had vertebral specimen found with lung cancer after surgery. No tumor cells were observed in 7 specimens of 5 patients (**Table 1**). In the other 23 patient without tumor history, 25 specimens of 17 patients (including matastasis and myeloma patients) were reported to be malignant while no tumor cells were seen in 8

**Table 5.** The diagnostic value of the MRI for malignant vertebral compression fractures

| MRI characteristics | Groups | | Sensitivity (%) | Specificity (%) | Accuracy (%) | +PV (%) | -PV (%) |
|---|---|---|---|---|---|---|---|
| | Malignant | Benign | | | | | |
| Posterior margin spherical bulge | 36/49 | 7/15 | 73.47 | 53.33 | 68.75 | 83.72 | 38.10 |
| Epidural mass | 39/49 | 3/15 | 79.59 | 80 | 79.69 | 92.86 | 54.55 |
| Pedicle involvement | 45/49 | 5/15 | 91.84 | 66.67 | 85.94 | 90 | 71.43 |
| Low T1 uniform signal | 44/49 | 9/15 | 89.80 | 40 | 78.13 | 83.02 | 54.55 |

Note: + PV: positive predictive value; - PV: negative predictive value.

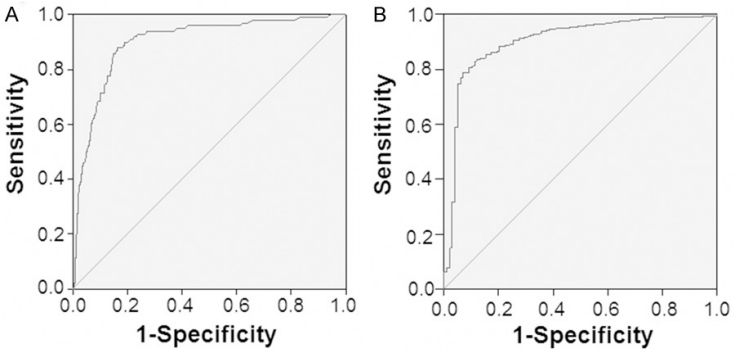


**Figure 4.** ROC curves for biopsy and MRI. A. ROC curve for biopsy. The AUC was 0.9. B. ROC curve for MRI. The AUC was 0.903.

specimens from 6 osteoporosis patients (**Table 2**).

In all 49 malignant vertebral lesions determined by biopsy, 46 malignant vertebral lesions and 3 suspected malignant vertebral lesions were diagnosed by MRI. However, 7 malignant and 8 suspected malignant vertebral lesions were diagnosed by MRI in all fractures with malignant vertebral excluded by biopsy (**Table 3**). The preoperative MRI studies were consistent with biopsy in diagnosis of malignant vertebral fractures (**Table 4**).

The sensitivity, specificity, and accuracy of MRI in diagnose of malignant vertebral fractures were calculated through comparing MRI results and pathological diagnosis results. The sensitivity, specificity, and accuracy of MRI for posterior margin spherical bulge were 73.47%, 53.33%, and 68.7%, respectively. The sensitivity, specificity, and accuracy of MRI for epidural mass were 79.59%, 80%, and 79.69%, respectively. The sensitivity, specificity, and accuracy of MRI for pedicle involvement were 91.84%, 66.67%, and 85.94%, respectively. The sensitivity, specificity, and accuracy of MRI for low T1 uniform signal were 89.80%, 40%, and 78.13%, respectively. As given in **Table 5**, the highest sensitivity, specificity, and accuracy occurred for epidural mass and pedicle involvement, while the lowest specificity and accuracy occurred for posterior margin spherical bulge and low T1 uniform signal. The ROC curve for biopsy and MRI was shown in **Figure 4A** and **4B**, respectively. The area under the curve (AUC) was 0.9 for biopsy and 0.903 for MRI. Altogether, the above results suggest that MRI was limited in the diagnosis of vertebral compression fractures and needed confirmation of pathological examination.

## Discussion

In this study, the high positive rates were obtained in diagnostic MRI for suspected malignant vertebral fractures. The causes of vertebral compression fractures may include metastasis of primary tumor or secondary osteoporosis due to long-term antitumor treatment. Although MRI can provide diagnostic information, vertebral puncture biopsy diagnosis can provide more useful information. Allen [18] suggested that vertebral puncture biopsy should be performed for all patients who underwent PKP. Shindle [21] also indicated that this technique should be used to all patients with vertebral compression fractures. It was reported that coaxial puncture biopsy had play a role in identifying the reason of vertebral compression fractures in percutaneous vertebroplasty [16]. It was shown that routine biopsy should be performed for each vertebral fracture [22].

The major complications of percutaneous vertebral puncture biopsy, such as spinal cord injury, vascular injury, hematoma, vertebral os-

teomyelitis, pneumothorax, and hemothorax had low incidences. Serial intraoperative monitoring, appropriate puncture point and aspiration were crucial for successfulness of treatment and reduction of the occurrence rates of complications. Our results suggest that percutaneous vertebral puncture biopsy and MRI are useful in diagnosis of malignant vertebral fractures. Thus, vertebral puncture biopsy and MRI should be performed for each patient with possible malignant vertebral fractures.

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## Disclosure of conflict of interest

None.

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