

Application of SPECT combined with CT and MRI in malignant tumors Clinical value in the diagnosis of bone metastasis

XIAO LI¹, WENDA SHI², FAN XU², QINGSHAN LI², XU XIAO³

Departments of ¹Radiology, ²Oncology and ³Pharmacy, Affiliated Hospital of Chengde Medical College

Abstract

Objective: To evaluate the value of single-photon emission computerized tomography (SPECT) combined with CT and MRI in the diagnosis of bone metastasis of malignant tumors.

Method: Eighty patients with bone metastasis from malignant tumors who admitted to Affiliated Hospital of Chengde Medical College were selected from March 2019 to June 2021. SPECT bone imaging, CT and MRI were used to analyze the regional distribution of primary tumor bone metastasis and the efficacy of three detection methods in the diagnosis of bone metastasis.

Results: A total of 464 lesions were detected by SPECT and CT in the same scanning field, with SPECT detection rate of 92. 5% (429 /464) and CT detection rate of 77. 8% (361 /464) ($P < 0. 05$). In addition, 143 lesions were detected by SPECT beyond the same scanning field. A total of 321 lesions were detected by SPECT and MRI in the same scanning field, with SPECT detection rate of 95. 6% (307 /321) and MRI detection rate of 82. 6% (265 /321) ($P < 0. 05$), and other 286 lesions were detected by SPECT beyond the same scanning field. In all, 259 lesions were detected by CT and MRI scans in the wild same scanning field. The detection rate was 71. 4% (185 /259) for CT, and 95. 7% (248 /259) for MRI($P < 0. 05$). The ensitivity, specificity and accuracy of SPECT imaging combined with CT and MRI were higher than single SPECT imaging, CT and MRI ($P < 0. 05$).

Conclusion: SPECT may be the preferred screening modality for suspected bone metastases, and when combined with CT and MRI, it can clarify the regional distribution of bone metastasis from malignant tumors and improve the sensitivity, specificity and accuracy of diagnosis with high clinical significance.

Key words: Bone scan with SPECT imaging; Malignant bone metastases; Computed tomography; Magnetic resonance imaging

Corresponding Author:

Fan Xu, Department of Oncology, Affiliated Hospital of Chengde Medical College, 36 Nanyingzi Street, Shuangqiao, Chengde, Hebei 067000, P.R. China. E-mail: 28574060@qq.com

Introduction

The definition of bone metastases is that tumors in any part of the body metastasize to the bone through various ways and continue to grow.¹ All tumor patients may have bone metastases.² The incidence of bone metastasis in breast³, prostate⁴, lung, thyroid⁵ and kidney cancer is more than 90%. The most common sites of bone metastases in China are spine, ribs, pelvis and femur. The clinical manifestations are systemic consumption symptoms, metastatic pain and pathological fractures.⁶ With the rapid development of imaging technology, the value and significance of imaging examination for early detection of bone metastases are gradually emerging. At present, the commonly used clinical examination methods include X-ray, computed tomography (CT), magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT). The imaging data of 80 cases of malignant tumor with bone metastasis were compared and analyzed to explore the application value of SPECT, CT and MRI in the diagnosis of bone metastasis.

Data and methods

1. General data: Eighty patients with bone metastasis from malignant tumors who admitted to Affiliated Hospital of Chengde Medical College were retrospectively selected from March 2019 to June 2021. The research method was approved by the hospital ethics committee. The patients and their

families were informed and signed the informed consent. Inclusion criteria: ① Patients with tumor history were confirmed by pathological examination or clinical diagnosis; ② Plane bone imaging was positive for the first time. Exclusion criteria: ① Contraindications of CT, MRI and SPECT; ② Patients with chronic organ failure; ③ psychiatric patients; ④ Patients with contrast medium allergy; ⑤ Patients with severe liver and kidney function and bone marrow dysfunction; ⑥ Survival time < 3 months. There were 46 males and 34 females, aged from 30 to 80 (60.23 ± 9.56) years; Primary cancer: 26 cases of lung cancer, 22 cases of breast cancer, 17 cases of prostate cancer, 3 cases of nasopharyngeal carcinoma, 4 cases of esophageal cancer, 2 cases of colon cancer and liver cancer, 1 cases of renal cell carcinoma, gastric cancer, colon cancer and cervical cancer. There were 46 males and 34 females, aged from 30 to 80 (60.23 ± 9.56) years; Primary cancer: 26 cases of lung cancer, 22 cases of breast cancer, 17 cases of prostate cancer, 3 cases of nasopharyngeal carcinoma, 4 cases of esophageal cancer, 2 cases of colon cancer and 2 cases of liver cancer, 1 case of renal cancer, 1 case of gastric cancer, 1 case of colon cancer and 1 case of cervical cancer.

2. Inspection method: To analyze the regional distribution of bone metastases and the accuracy of SPECT bone imaging combined with CT and MRI in the diagnosis of bone metastases. (1) SPECT bone imaging: Infinia dual probe SPECT instrument with a low-energy high-resolution collimator provided by GE company of the United States was used. After intravenous injection of ^{99m}Tc methylene diphosphate (^{99m}Tc MDP) for 20 ~ 25 mci, the patient drank 600 ~ 1000ml water, and the bladder was emptied after 3 hours, and performed anterior posterior and posterior anterior whole-body bone imaging at a speed of 15cm / min. Then the whole body bone imaging was performed at a speed of 15 cm / min. (2) CT examination: discovery hd 750 multi-slice spiral CT provided by GE company of the United States was used, with layer thickness of 5 ~ 10 mm, and soft tissue window and bone window were used for observation. (3) MRI examination: discovery MR 750 3.0 nuclear magnetic resonance produced by GE company in the United States, conventional spin back sequence was used for cross-sectional, coronal and sagittal T1WI and T2WI imaging. (4) Image analysis and result judgement: the diagnosis was made by more than two experienced radiologists and nuclear medicine doctors. The gold standard for the diagnosis of bone metastasis is histopathological examination, but it is unrealistic to

perform trucut biopsy for each patient. The diagnostic criteria for bone metastases used in this study are⁷: ① bone metastases confirmed by pathological examination. ② There are two or more imaging methods to diagnose bone metastases. ③ After follow-up for more than 6 months, the lesions increased or decreased after anti-tumor treatment. Those who met one of the three conditions were diagnosed as bone metastases.

3. Statistical methods: SPSS 20.0 software was used for data processing, and the measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Using t-test, the counting data were expressed in rate (%). Using χ^2 -test, the difference was statistically significant ($P < 0.05$).

Results

1. Analysis of clinical manifestations: there were 46 cases without bone pain symptoms and 34 cases with bone pain. Bone metastases occurred in the spine, ribs, pelvis, chest, limbs and skull. Among spinal metastases, the most common sites were thoracic vertebrae, lumbar vertebrae, sacral vertebrae and cervical vertebrae, table 1.
2. Comparison of detection rate of bone metastasis by SPECT, CT and MRI: A total of 464 lesions were detected by SPECT and CT in the same scanning field, with SPECT detection rate of 92.5% (429 / 464) and CT detection rate of 77.8% (361 / 464), the

difference was statistically significant ($X^2 = 39.36$, $P < 0.05$). In addition, 143 lesions were detected by SPECT beyond the same scanning field.

Table 1: Distribution area of bone metastasis caused by malignant tumor

Distribution area of bone metastasis	Number of cases	Number of lesions
spine	63	166
ribs	48	155
pelvis	32	113
chest (sternum, clavicle, scapula)	21	80
limbs	17	72
skull	9	21

- A total of 321 lesions were detected by SPECT and MRI in the same scanning field, with SPECT detection rate of 95.6% (307/321) and MRI detection rate of 82.6% (265/321), the difference was statistically significant ($X^2 = 28.48$, $P < 0.05$), and other 286 lesions were detected by SPECT beyond the same scanning field. In all, 259 lesions were detected by CT and MRI scans in the wild same scanning field. The detection rate was 71.4% (185/259) for CT, and 95.7% (248/259) for MRI, the difference was statistically significant ($X^2 = 69.86$, $P < 0.05$).
- Comparison of SPECT bone imaging, CT and MRI in the diagnosis of bone metastases: The

sensitivity, specificity and accuracy of SPECT combined with CT and MRI were significantly higher than those of SPECT bone imaging, CT or MRI alone ($P < 0.05$), table 2.

Table 2: Comparison of SPECT, CT and MRI in the diagnosis of bone metastases (%)

Inspection items	Sensitivity	Specificity	Accuracy
SPECT	92.6	70.8	79.5
CT	83.8	88.7	86.5
MRI	90.6	89.2	89.5
Combination of three inspections	98.7	92.5	95

Discussion

The incidence of malignant tumor metastasis to bone is so high, but many patients have no symptoms of bone pain. In this study, 80 patients with bone metastasis of malignant tumor, 46 cases had no obvious symptoms of bone pain and 34 cases had obvious symptoms of bone pain. The main ways of metastasis of malignant tumors were hematogenous dissemination, lymphatic metastasis and local infiltration. Most tumor cells were transferred to the bone system through blood dissemination, and a few tumor cells were directly transferred to the bone through soft tissue. Some scholars believed that red bone marrow was suitable for the reproduction of tumor cells in hemodynamics and biochemistry, so it had become the preferred site for tumor cell

metastasis^[8], and more than 90% of bone metastases were located in the axial bone with more red bone marrow^[9]. The results of this study showed that most bone metastases were located in the axial bone and the proximal end of the long bones of the limbs with more red bone marrow. Bone metastases occurred in the spine, ribs, pelvis, chest, limbs and skull. Among them, the incidence of spinal metastases was high, which might be related to Batson venous plexus. Batson theory believed that the spinal venous plexus was connected with the thoracic, abdominal and pelvic venous plexus, where the blood flow was slow and there was no venous valve obstruction. When the thoracic and abdominal pressure increases due to respiratory movement, the tumor cells directly retrograded into the spine through the spinal venous plexus. This study also showed that the most common sites of spinal metastases were thoracic vertebrae, lumbar vertebrae, sacral vertebrae and cervical vertebrae, which was considered to be related to the fact that the primary tumors were mostly in the chest and abdomen.

SPECT is one of the most commonly used methods for the diagnosis of bone metastasis of malignant tumors, which uses radionuclide technetium labeled methylene bisphosphonate (^{99m}Tc MDP) as imaging agent to display the difference of radioactive concentration in image form by single photon emission tomography^[10]. SPECT showed that most bone metastases were multiple and

asymmetric radioactive concentrated foci, and a few osteolytic metastases showed cold areas of radioactive defects. SPECT has a high sensitivity to early metastases, which is half a year or even a year earlier than X-ray examination. In addition, SPECT can examine the whole body bone at one time, which greatly reduces the possibility of missed diagnosis. SPECT is also used to assist the localization of radiotherapy and evaluate the curative effect.¹¹ CT is sensitive to detect the destruction of bone cortex, but intramedullary metastases without bone cortex destruction which often shows small low-density lesions in the medullary cavity, is easy to miss diagnosis.¹² The important value of CT is to evaluate the uncertain lesions in SPECT, and can accurately detect the location, diameter and shape of the lesions. In this study, bone metastases showed 3 forms: osteogenic type, osteolytic type and mixed type. Bone metastases of prostate cancer mostly showed osteogenic type. Bone metastases of liver cancer mostly showed osteolytic type, and bone metastases and osteolytic types were mostly seen in lung cancer and breast cancer. CT can show the surrounding situation, blood supply and adjacent soft tissue of the metastasis which is helpful to judge whether there are complications of malignant tumor bone metastasis, such as pathological fracture, spinal cord compression and so on. CT can also help to identify benign and malignant

vertebral compression, whether there is involvement of vertebral appendages, whether it breaks through bone to form soft tissue mass, etc.¹² Bone metastases of malignant tumors start from bone marrow. The occurrence of intra-medullary metastases will lead to changes in bone marrow fat and water content in varying degrees. MRI is very sensitive to the changes of fat and water content, and MRI has high spatial resolution, which is of great value in the early diagnosis of bone metastases. In this group of data, most of the MRI positive cases showed long T1 and long T2 signals. MRI detected more early intra-medullary metastases than SPECT and CT. This study showed that the detection rate of bone metastases by MRI was higher than that by SPECT and CT. In reality, MRI scanning range was limited, which was difficult to check the whole body's bone condition, and it was easy to be affected by artifacts caused by breathing and heart beat movement, resulting in missed diagnosis of rib and thoracic vertebral lesions. In this study, the sensitivity, specificity and accuracy of SPECT bone imaging combined with CT and MRI were significantly higher than those of SPECT, CT or MRI alone. In conclusion, SPECT can be used as a preliminary screening method for bone metastases. Combined with CT and MRI, SPECT can clarify the regional distribution of bone metastases of malignant tumors, improve the sensitivity, specificity and accuracy of diagnosis, and has high clinical value.

Reference

1. Zhao Zhiqing, ye Zhipeng, Yan taiqiang, et al. Research progress in quality of life assessment of patients with bone metastases[J]. Chinese Journal of Orthopaedics, 2017, 37: 1177-1184
2. Zhu Anhui, Wang Rongfu. Comparison of PET / CT and whole body bone imaging in the diagnosis of different types of bone metastases[J]. China medical imaging technology, 2016, 32: 944-948
3. Yang Zhi, Yang Guisheng, Lining, et al. Diagnostic value of whole-body bone imaging combined with CA153 and CEA in breast cancer with bone metastasis [J]. Chinese Journal of cancer prevention, 2016, 23: 1229-1233.
4. Zhang Linqi, Qin Yifang, Li Wei, et al. Diagnosis of bone metastasis in patients with high-risk prostate cancer by conventional SPECT / CT tomography fusion imaging [J]. China medical imaging technology, 2017, 33: 260-264
5. Sheng Fangjun, Wang Mian, Yang Lu, et al. Comparative analysis of 131 I and chemoradiotherapy in the treatment of bone metastasis of differentiated thyroid cancer and its impact on the survival of patients [J]. Chinese Journal of endemic disease prevention and control, 2016, 31: 131-133.
6. Xiong Hairui, Zhou Qian, Zhang Junhai, et al. Short term efficacy and safety of Mr guided focused ultrasound in relieving pain of bone metastases [J]. Chinese Journal of Radiology, 2017, 51: 446-450
7. Ding yueyun, Shi Dedao, Zhu Zongping, et al. Study on the value of SPECT / CT bone tomographic fusion imaging in the diagnosis of tumor bone metastasis [J]. Journal of medical imaging, 2017, 27: 527-530
8. Niu YJ, Wen YT, Shen WW, et al. Risk factors for bone metastasis in patients with primary lung cancer: study protocol for a systematic review[J]. BMJ Open, 2014, 4: e005202
9. Li Lin, Zhao Zhen, Guo Xing. Imaging diagnosis of malignant tumor bone metastasis[J]. Chinese Journal of nuclear medicine, 2006, 26: 315-318
10. Zhao Hui, an Jianping, Xu Xiaohong, et al. Evaluation of bone metastasis of prostate cancer by radionuclide bone imaging

- combined with PSA, FPSA and FPSA / TPSA [J]. Journal of radioimmunology, 2011, 24: 176-178
11. Wang Shejiao, song Yangrong, Zheng Xianghong, et al. Evaluation of the efficacy of ¹⁵³Sm EDTMP in the treatment of bone metastases by whole body bone imaging [J]. Modern oncology medicine, 2008, 16: 2177-2179
 12. You Meiqin, Wang Shouhua, Jiang congfei, et al. Clinical analysis of radioactive I¹²⁵ seed implantation in patients with advanced malignant tumors after radiotherapy and chemotherapy [J]. China cancer clinic and rehabilitation, 2018, 25: 102-104