Pathol. Oncol. Res. (2016) 22:79–85
DOI 10.1007/s12253-015-9975-y

ORIGINAL ARTICLE

Pattern of Tumour Spread of Common Primary Tumours as Seen on Magnetic Resonance Imaging

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Received: 13 February 2015 / Accepted: 24 August 2015 / Published online: 30 August 2015

Abstract Although some reports with computed tomography and bone scintigraphy are available in the literature, the distinct epidemiologic description of skeletal metastatic pattern of various tumors is still lacking. This study uses a novel approach to identify skeletal metastases from magnetic resonance imaging (MRI) data to describe metastatic pattern in common malignancies. A retrospective analysis of 130 cancer patients (42 lung, 56 breast, 11 prostate cancers; 21 multiple myeloma) with vertebral metastases and without disseminated disease, and whom underwent a whole body 3Tesla MRI investigation (Discovery MR750w), was carried out. Multiple myeloma had the most commonly disseminated metastatic disease (95 %) compared to lung (28 %), breast (44 %) and prostate (71 %) cancers. Lung cancer was related to more frequent pedicle involvement compared to breast or prostate cancer (29, 9 and 0 %, $p<0.05$). Pathologic fracture was mainly associated with multiple myeloma (43 %). The prevalence of lung cancer metastases was more frequent in the lumbal spine (81 %), as well as particular in C7, D7, D8, D9 and L1, compared to breast cancers. Most differences among tumors were detected in the extravertebral osseous metastatic pattern ($p<0.05$). The highest frequency of extravertebral skeletal metastases was present in multiple myeloma (28 to 76 %). Brain metastasis was more frequent in lung cancer compared to breast cancers (35 % vs. 17 %, $p<0.05$). Significant differences in the skeletal metastatic pattern among common malignancies were demonstrated with MRI.

Keywords Lung cancer · Breast tumor · Vertebral metastasis · Spine · Pedicle

Introduction

The global burden of cancer is growing [1]. Vertebral metastases occur between 5 and 10 % in cancer patients, especially in frequent malignant tumors, such as breast, prostate and lung cancer [2–5]. Bone metastases have prognostic impact and are significantly related to increased morbidity [6, 7]. The frequency of osseous metastases is 8 % in breast cancer patients and 69 % in patients with advanced disease [8]. In the case of lung cancer, about one third of all patients develop bone metastasis during the course of the disease [9]. Similarly, osseous metastases represent the most common metastatic site in advanced prostate cancer [10]. Consequences of bony metastases include pathologic fracture, spinal cord compression, anemia, and hypercalcemia [11]. The thoracic spine is the most common region involved in spinal metastases (70 %) [12].

Although often asymptomatic, the first main sign of skeletal metastases is pain [13]. On the course of the diagnostic algorithm of skeletal metastases, different methods are available [13]. Nowadays, magnetic resonance imaging (MRI) is the gold-standard imaging modality of metastatic spinal tumors, with superior sensitivity to standard radiographs, computed tomography, and bone scintigraphy due to its better soft-tissue resolution [14]. Additional advantages of MRI include the ability of defining important preoperative parameters (e.g.,

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extent of epidural extension, degree of spinal cord compression, surrounding edema, spinal root impingement) and the evaluation of neighboring structures (e.g., joints, ligaments, paraspinal muscles). The use of gadolinium contrast could enhance the information on soft-tissue infiltration and vascularity [15]. Although the sensitivity of MRI high, the specificity is lower, which can be further enhanced by a comprehensive analysis of metastatic pattern. A recent report with bone scintigraphy is available in the literature [16], but the metastatic pattern has not yet been analysed by MRI. Therefore, in the present study, we investigated the distribution of bone metastases in common malignancies using MRI.

Methods and Materials

Subjects and Study Protocol

We carried out a retrospective analysis of all patients who underwent whole body skeletal MRI at the Institute of Diagnostic and Interventional Radiology, Caritasklinikum Saarbrücken St. Theresia, Germany on a Discovery MR750w 3 Tesla wide bore device (General Electric Healthcare, GE, Milwaukee, USA; 70 cm wide bore magnet) between July 2012 and July 2014 using a picture archiving and communication system (AGFA IMPAX and KIS-RIS ORBIS, AGFA Healthcare, Mortsel, Belgium) in order to select patients with vertebral metastases. Lung, breast and prostate cancer were the most frequent malignancies. 231 histologically proven cancer patients, including 58 lung cancer, 100 breast cancer, 34 prostatic cancer, 21 multiple myeloma (plasmacytoma) and 18 gastrointestinal tumors (appendix cancers, gastrointestinal stroma tumor, colon cancers, rectum, oesophageal and gastric cancers) (132 females, 99 males, age 66.8±11.5 years) were identified. We excluded patients with disseminated disease in lung, breast, prostatic and gastrointestinal tumors, where the number of metastases was uncountable. We also excluded all gastrointestinal tumor patients because of the heterogeneity of the tumors and the low number of vertebral metastases which made the comparison with other tumors impossible. Since most of the patients with multiple myeloma had disseminated disease, all of the cases were analysed as if the variables were countable or dichotomous. Finally, 130 subjects (42 lung cancer, 56 breast cancer, 11 prostate cancer and 21 multiple myeloma) of which were 78 females and 52 males (mean age 66.0±11.7 years), were included in the analysis. Patients with uncertain histological findings or multiple cancers were also excluded. The whole body MRI protocol was identical for all subjects and included a sagittal T1 and short tau inversion recovery (STIR) of the entire vertebral skeleton, a coronal T1 of the thorax (including the sternum, clavicles, proximal humeri and ribs bilaterally), an axial T1 of the pelvis, and a coronal T1 sequence of the proximal femora.

Image and Statistical Analysis

Both the images and reports of the patients were carefully reviewed and each bone metastasis was registered as dichotomous variables. The presence of bone metastasis in the vertebral pedicles, transverse and spinous processes, complete vertebral body involvement, vertebral or closing plate fracture and metastases in the sternum, pelvic bone, sacrum, clavicles, proximal humerus und femur, ribs and in parenchymal organs (lung, brain, liver) were also registered. The patient records were also checked in order to find imaging studies (computed tomography, MRI, ultrasound) or other evidence for lung, liver and brain metastases. Cases without imaging evidence for metastases were not included in the analysis. Chi square test was applied for comparison of the variables using SPSS Statistics Version 16. A p-value of <0.05 was taken to be statistically significant. If the expected frequency was below 1 or less than 5 in more than 20 % of the cells, Chi square test was not run and comparison was not possible.

Results

Prevalence of Disseminated Disease, Osseous Lesions and Occurance of Vertebral Metastases According to Spine Regions

Significant differences were noticed in disseminated disease among various tumors ($p=0.000$, Table 1). Multiple myeloma was almost in all cases disseminated, while prostate cancer was significantly more disseminated than lung and breast cancers ($p<0.05$). There was a tendency that the presence of complete vertebral body involvement, and the involvement of the spinous and transverse processes were more likely to be affected by lung cancer as opposed to breast and prostate cancer, however, no significance could be calculated due to the low number of cases ($p<0.05$). Pedicle involvement was significantly more frequent in lung cancer than in breast or prostate cancer (29 % vs. 9 % and 0 %, $p<0.05$). Vertebral or closing plate fracture was highly associated with multiple myeloma compared to lung cancer ($p<0.05$). The prevalence of lung cancer metastases was more frequent in the lumbal spine (81 %) compared to breast cancer. No significant difference was observed in the metastatic involvement of the cervical and thoracic spinal regions among the investigated cancer types.

Prevalence of Vertebral Metastases According to Each Vertebrae

Lung cancer metastases were predominantly present in vertebrae C7, D7, D8, D9 and L1 compared to breast cancer

Table 1 Prevalence of disseminated disease, osseous lesions and total number of vertebral metastasis according to spine regions in lung, breast and prostate cancers and multiple myeloma with *p* values between groups with significance values using Chi square tests (excluding cases in which information was not available on metastases)

	Prevalence in lung cancer, n (%) (*n*=42)	Prevalence in breast cancer, n (%) (*n*=56)	Prevalence in prostate cancer, n (%) (*n*=11)	Prevalence in multiple myeloma, n (%) (*n*=21)	p-value of Chi square test between groups
Disseminated disease (n/total n)	16/58 (27.6 %)*†‡‡	44/100 (44.0 %)*$	24/34 (70.6 %)†¶§	20/21 (95.2 %)‡‡$¶	0.000
Lesion in pedicle	12 (28.6 %)*	5 (8.9 %)*	0 (0.0 %)	N/A	0.064μ
Lesion in transverse process	4 (9.5 %)	1 (1.8 %)	1 (9.1 %)	N/A	N/Aβ
Lesion in spinous process	7 (16.7 %)	3 (5.4 %)	1 (9.1 %)	N/A	N/Aβ
Complete vertebral body involvement	3 (7.1 %)	1 (1.8 %)	0 (0.0 %)	N/A	N/Aβ
Vertebral or closing plate fracture	7 (16.7 %)‡	8 (14.3 %)	3 (27.3 %)	9 (42.9 %)‡	0.016π
Total number of patients with cervical vertebral metastases	12 (28.6 %)	9 (16.1 %)	5 (45.5 %)	N/A	0.074£
Total number of patients with thoracic vertebral metastases	34 (80.9 %)	39 (69.6 %)	7 (63.6 %)	N/A	0.338£
Total number of patients with lumbal vertebral metastases	33 (80.9 %)*	33 (58.9 %)*	7 (63.6 %)	N/A	0.119€

*$p<0.05$ between lung and breast cancer; † $p<0.01$ between lung and prostate cancer; ‡ $p<0.05$ between lung cancer and multiple myeloma; ‡‡ $p<0.01$ between lung cancer and multiple myeloma; $ $p<0.01$ between breast cancer and multiple myeloma; ¶ $p<0.05$ between prostate cancer and multiple myeloma. Significance levels between breast and prostate cancers are not shown. Multiple myeloma group includes cases of disseminated disease, whileas other groups do not contain cases with disseminated disease. NA, non applicable, cases of vertebral metastases are not shown in case of multiple myeloma due to the disseminated nature of the disease. β Chi square test was not run due to the low frequency of lesions. μ *p* value without prostate cancer and multiple myeloma due to the low frequency of lesions in these tumors. π *p* value without prostate cancers due to the low frequency of lesions in these tumors – no *p* values were calculated with these tumors as well as between breast cancer and multiple myeloma for the same reason in the same row. £ *p* value without multiple myeloma due to the low frequency of lesions in these tumors – no *p* values were calculated among all tumors separately for the same reason in the same row. € *p* value without multiple myeloma due to the low frequency of lesions in these tumors – no *p* values were calculated between prostata cancer and all other tumors separately for the same reason in the same row

($p<0.05$), especially in D7, which was very significant ($p=0.000$) (Table 2). The low sample size of prostate tumors did not allow the comparison between groups in most cases.

Prevalence of Extravertebral Osseous and Non-Osseous Metastases According to Each Vertebrae

Most differences among tumors were detected in the pattern of extravertebral osseous metastases ($p<0.05$) (Table 3). The highest frequency of extravertebral osseous metastases was found in multiple myeloma (28 to 76 %). Brain metastasis was more frequent in lung cancer compared to breast cancers (35 % vs. 17 %, $p<0.05$). Lung cancer metastases were more prevalent compared to that of breast cancer and multiple myeloma ($p<0.05$).

Discussion

In this study, we demonstrated significant differences in the pattern of vertebral osseous, extravertebral osseous, and non-osseous metastatic involvement among lung, breast, prostate cancers and multiple myeloma using MR imaging.

In line with our study, lung, breast and prostate cancers have been described as the most common primary sources for developing skeletal metastases [17, 18]. Accordingly, we analysed these most frequent malignancies resulting in vertebral metastases. We have shown that almost in all cases of multiple myeloma (plasmocytoma), the lesions appeared disseminated in MRI, which did not allow us to compare these cases with vertebral metastases of other common malignancies. MRI for examining vertebral infiltration of multiple myeloma has been reported to be superior to all other imaging methods in demonstrating changes in bone marrow [19]. We also showed that prostate cancer is more likely to be disseminated than lung and breast cancers. Bone metastases of prostate cancer are common. Bubendorf et al. reported that prostate cancers gave metastases in 35 % of cases, 90 % which were bone metastases according to autopsy findings [20].

To our knowledge, it has never been demonstrated that the involvement of the pedicle is more likely to be affected by lung cancer than breast cancer. We suspect that this phenomenon can be related to the metastatic spreading mechanism of the tumor cells. In general, the pedicle is a common place of early metastatic involvement because of the ability of tumor cells to spread through anatomic arterial supplies of vertebrae [21–23]. However, pedicles are not the primary sites of

Table 2 Prevalence of vertebral metastases according to each vertebrae in lung, breast and prostate cancers and multiple myeloma with *p* values between groups with significance values using Chi square tests (excluding cases in which information was not available on metastases)

	Prevalence in lung cancer, n (%) (*n*=42)	Prevalence in breast cancer, n (%) (*n*=56)	Prevalence in prostate cancer, n (%) (*n*=11)	Prevalence in multiple myeloma, n (%) (*n*=21)	*P*-value of Chi square test between groups
C1	1 (2.4 %)	0 (0.0 %)	0 (0.0 %)	N/A	N/A$^{\beta}$
C2	5 (11.9 %)	1 (1.8 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
C3	2 (4.8 %)	1 (1.8 %)	0 (0.0 %)	N/A	N/A$^{\beta}$
C4	1 (2.4 %)	0 (0.0 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
C5	2 (4.8 %)	3 (5.4 %)	2 (18.2 %)	N/A	N/A$^{\beta}$
C6	2 (4.8 %)	2 (3.6 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
C7	7 (16.7 %)*	6 (10.7 %)*	1 (9.1 %)	N/A	0.038$^{\mu}$
D1	6 (14.3 %)	2 (3.6 %)	2 (18.2 %)	N/A	N/A$^{\beta}$
D2	8 (19.0 %)	3 (5.4 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
D3	5 (11.9 %)	8 (14.3 %)	1 (9.1 %)	N/A	0.731$^{\mu}$
D4	6 (14.3 %)	9 (16.1 %)	0 (0.0 %)	N/A	0.808$^{\mu}$
D5	7 (16.7 %)	1 (1.8 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
D6	7 (16.7 %)	4 (7.1 %)	1 (9.1 %)	N/A	N/A$^{\beta}$
D7	14 (33.3 %)**	2 (3.6 %)**	2 (18.2 %)	N/A	0.0004$^{\pi}$
D8	10 (23.8 %)*	5 (8.9 %)*	4 (36.3 %)	N/A	0.034$^{\pi}$
D9	12 (28.6 %)*	7 (12.5 %)*	2 (18.2 %)	N/A	0.121$^{\mu, \epsilon}$
D10	2 (4.8 %)	9 (16.1 %)	2 (18.2 %)	N/A	0.185$^{\pi}$
D11	6 (14.3 %)	10 (17.9 %)	1 (9.1 %)	N/A	0.636$^{\mu}$
D12	10 (23.8 %)	13 (23.2 %)	2 (18.2 %)	N/A	0.922$^{\pi,£}$
L1	16 (38.1 %)*	10 (17.9 %)*	3 (27.3 %)	N/A	0.081$^{\pi, \epsilon}$
L2	14 (33.3 %)	13 (23.2 %)	2 (18.2 %)	N/A	0.427$^{\pi, \epsilon}$
L3	14 (33.3 %)	13 (23.2 %)	3 (27.3 %)	N/A	0.540$^{\pi, £}$
L4	12 (28.6 %)	12 (21.4 %)	3 (27.3 %)	N/A	0.705$^{\pi, £}$
L5	11 (26.2 %)	12 (21.4 %)	2 (18.2 %)	N/A	0.828$^{\mu, £}$

*$p<0.05$ between lung and breast cancer; **$p<0.01$ between lung and breast cancer. Significance levels between breast and prostate cancers are not shown. Multiple myeloma group includes cases of disseminated disease, whileas other groups do not contain cases with disseminated disease. NA, non applicable, cases of vertebral metastases are not shown in case of multiple myeloma due to the disseminated nature of the disease. $^{\beta}$ Chi square test was not run due to the low frequency of lesions. $^{\mu}p$ value without prostate cancer and multiple myeloma due to the low frequency of lesions in these tumors. $^{\pi}p$ value without multiple myeloma due to the low frequency of lesions in these tumors. $^{£}p$ values were calculated among tumors separately due to the low frequency of lesions in some tumors. $^{\epsilon}p$ values were not calculated between prostate cancer and multiple myeloma with other tumors separately due to the low frequency of lesions in these two tumors

metastatic involvement, since the vertebral pedicle mainly consists of cortical bone and virtualy no bone marrow. This is in contrast with the vertebral body, which is more likely to harbor and develop metastases than other parts of the vertebra [24]. A computed tomography study has shown that the initial anatomic location of metastases within vertebrae is in the posterior portion of the body. This is significant because the destruction of a pedicle never happens in the absence of involvement of the body [25]. The position of the metastases in the vertebra correlates with the sites of entry of the vertebral vessels [25]. However, pedicle involvement is still an important MRI marker of malignant fractures, which helps in the differentiation between malignant, osteoporotic, and infective vertebral compression fractures [26]. An experimental study has shown that cancer cells in the vertebral marrow cavity invade into the spinal canal through the foramina of the vertebral veins, toward a posterior location, rather than destroying the cortical bone [27]. The occurance of metastatic involvement of pedicles in lung cancers is in line with previous observations, accounting for around 30 % of cases [25]. This indicates that not only lung cancers are more likely to give metastases to the pedicles, but breast (and, however not statistically proven, but probably prostate cancer as well) metastases are less likely to effect the pedicles. Our results are further supported by a previous investigation which showed that involvement of the pedicle is by direct extension from either the vertebral body, or its posterior elements, and therefore is a late occurrence in the disease process in breast cancer patients [28]. Nevertheless, studies on molecular and cellular biological characteristics of tumor cells are necessary to support our findings [29–31].

Table 3 Prevalence of extravertebral osseous and non-osseous metastases in lung, breast and prostate cancers and multiple myeloma with *p* values between groups with significance values using Chi square tests (excluding cases in which information was not available on metastases)

	Prevalence in lung cancer, n (%) (*n*=42)	Prevalence in breast cancer, n (%) (*n*=56)	Prevalence in prostate cancer, n (%) (*n*=11)	Prevalence in multiple myeloma, n (%) (*n*=21)	*P*-value of Chi square test between groups
Sacrum metastasis	19 (45.2 %)	18 (32.1 %)$^{\$\$}$	4 (36.3 %)	15 (71.4 %)$^{\$\$}$	0.039$^{\mu}$
Pelvic bone metastasis	25 (59.5 %)	26 (46.4 %)$^{\$}$	8 (72.7 %)	16 (76.2 %)$^{\$}$	0.010$^{\pi}$
Sternal metastasis	10 (23.8 %)‡‡	9 (16.1 %)$^{\$\$}$	4 (36.3 %)	13 (61.9 %)$^{\ddagger\ddagger\$\$}$	0.000
Humerus metastasis	11 (26.2 %)‡‡	7 (12.5 %)$^{\$\$}$	3 (27.3 %)¶	16 (76.2 %)$^{\ddagger\ddagger\$\$\P}$	0.000
Clavicle metastasis	5 (11.9 %)‡‡	6 (10.7 %)$^{\$\$}$	2 (18.2 %)¶	14 (66.7 %)$^{\ddagger\ddagger\$\$\P}$	0.000$^{\pounds}$
Rib metastasis	9 (21.4 %)‡‡	8 (14.3 %)$^{\$\$}$	3 (27.3 %)	12 (57.1 %)$^{\ddagger\ddagger\$\$}$	0.001
Femur metastasis	20 (47.6 %)‡	19 (33.9 %)$^{\$\$}$	1 (9.1 %)	17 (81.0 %)$^{\ddagger\$\$}$	0.000$^{\epsilon}$
Lung metastases	20 (51.3 %)*‡‡	13 (25.0 %)*	1 (12.5 %)	1 (5.9 %)‡‡	0.002$^{¥}$
Liver metastases	11 (31.4 %)	10 (21.3 %)	1 (12.5 %)	1 (5.9 %)	0.558$^{\Omega}$
Brain metastases	12 (35.3 %)*	5 (17.2 %)*	1 (25.0 %)	0 (0.0 %)	0.040$^{\Omega}$

*$p<0.05$ between lung and breast cancer; $^{\ddagger}p<0.05$ between lung cancer and multiple myeloma; $^{\ddagger\ddagger}p<0.01$ between lung cancer and multiple myeloma; $^{\$}p<0.05$ between breast cancer and multiple myeloma; $^{\$\$}p<0.01$ between breast cancer and multiple myeloma; $^{\P}p<0.01$ between prostate cancer and multiple myeloma. Significance levels between breast and prostate cancers are not shown. $^{\mu}p$ values between lung cancer and all other cancers, prostate cancer with multiple myeloma were not calculated due to the low frequency of lesions in some of these tumors. $^{\pi}p$ values between lung cancer and prostate cancer, between prostate cancer and multiple myeloma were not calculated due to the low frequency of lesions in some of these tumors. $^{\pounds}p$ value does not include prostate cancer, and *p* values were calculated between lung and breast cancer and between lung and prostate cancer separately due to the low frequency of lesions in some of these tumors. $^{\epsilon}p$ values were not calculated between breast and prostate cancer and between prostate cancer and multiple myeloma separately due to the low frequency of lesions in some of these tumors. $^{¥}p$ values were not calculated between lung and prostate cancer, between breast cancer and multiple myeloma and between prostate cancer and multiple myeloma separately due to the low frequency of lesions in some of these tumors. $^{\Omega}p$ values were not calculated including prostate cancer and multiple myeloma due to the low frequency of lesions in these tumors

Mechanisms such as tissue specificity, cascade system, and closed loop circulation system, may be also involved [32]. Establishment of various human cancer cell models with bone metastasis potential would be helpful in improving the understanding of not only the pathophysiology and the molecular mechanisms behind the spread of metastatic cancer to the spine, but also the signal regulation of organ-specific metastases, with the aim of developing new techniques and molecular targeting drugs of inhibiting or reversing bone metastasis [17, 33].

In our cohort, subjects with multiple myeloma had significantly higher prevalence of vertebral or closing plate fractures compared to lung cancer. Breast cancer had also a lower frequency compared to multiple myeloma, however, it was not statistically significant. A 9-fold increase in pathologic fracture risk in patients with multiple myeloma was demonstrated in the large study of Melton et al., especially around the time of diagnosis of myeloma in the vertebrae and ribs [34]. The prevalence of malignant compression fractures was even higher in a recent paper in patients newly diagnosed with multiple myeloma compared to our findings (88.5 % vs. 42.9 %) [35]. The authors concluded that spine MRI at the time of diagnosis is useful for detecting skeletal lesions and predicting the prognosis in patients with multiple myeloma [35]. Prostate cancer is known to have high rate of pathologic vertebral fractures, which was reported to be around 37 %, similar to our findings (27 %) [36].

In the same regard, the different metastatic involvement of vertebral bodies is another interesting phenomenon to consider. The more frequent prevalence of lung cancer metastases in the lumbal spines was observed compared to breast cancers. Moreover, more frequent occurence of lung cancer metastases was found in vertebrae C7, D7, D8, D9 and L1 compared to breast cancers. There was a tendency of higher frequency of patients with thoracic vertebral metastases in comparison with other tumors. The preference for thoracic spine metastatic involvement in comparison to cervical and lumbal spine, has been reported previously in general [37, 38] and also in lung cancer in particular [39]. However, limited detailed analysis is available regarding which vertebras are more likely to be affected by metastases of different primary malignancies. The Batson's vertebral venous plexus draining the thoracic viscera can be one other possible explanation of this phenomenon because it is a direct route of metastases to the axial skeleton throughout the epidural and perivertebral veins, especially for lung cancer [39, 40]. In addition, the increased frequency of spinal metastases in the thoracic vertebrae, compared to other regions, can be attributed to the greater number of thoracic vertebrae in general. Breast cancer metastasizes through the azygos communicates, to the plexus of Batson in the thoracic region, which is not a direct path as in lung cancer [40]. In prostate cancer, a backward metastatic pathway, leading from the prostate to the periprostatic and presacral veins, pelvic plexus, column, and subsequently to the lungs (in addition

to classical hematogeneous tumor spread via the vena cava) was also suggested. This might be explained by the gradual decrease of spinal involvement from the lumbar to the cervical level through upward metastatic spread along spinal veins after initial lumbar metastasis [41–44]. Our results support these hypotheses, that in the case of prostate cancer, there are more frequent metastases in lumbar and thoracic spine (both 64 %) compared to cervical spine (46 %). In the study of Moreno et al., spinal cord involvement most often occured in smaller tumors (4 to 6 cm), while lung involvement was more likely in large tumors (6 to 8 cm), with liver involvement usually restricted to the largest tumors (8 cm or larger) [42]. This suggested that spinal metastases precede lung and liver metastases based on tumor sizes [42]. Although the tumor cell diffusion through Batson venous system is the principal process of spinal metastasis, dissemination through the arterial and lymphatic system, or by contiguity, is also a possibility [45]. Aydinli et al. reported that the most common metastasis of lung cancer is D9 level in the thoracic region, which is partly in line with our observation [39]. In our study, the most significant difference between lung cancer and breast cancer was the presence of metastasis in D7 in lung cancer.

Extravertebral osseous metastases were more commonly differed among tumors as the vertebral ones. The highest frequency of extravertebral osseous metastases was found in multiple myeloma, which is in line with its known diffuse metastatic pattern in bones. On the other hand, no significant differences in the extravertebral osseous metastatic pattern was found among lung, breast and prostate cancer. In a recent review of pattern and distribution of bone metastases in common malignant tumors, spine, and pelvis in prostate carcinoma, and the spine, ribs, and sternum in breast carcinoma, as well as ribs and spine in lung cancer, are most frequently invaded [16]. In this study, no significant difference was found between the prevalence of femoral metastases in breast, prostate, and lung cancer (5 % vs. 6 % and 0 %), which is in line with our findings [16]. Another study demonstrated a 6 % prevalence of femoral metastasis in lung cancer patients, confirmed by radiography or bone scintigraphy [46]. However, prevalence of extraskeletal metastases in patients with vertebral metastasis remained unclear until this report.

Finally, our study assessed the presence of non-osseous metastases in patients with existing vertebral metastases. We found that brain metastases were more frequent in patients with existing vertebral metastases from lung cancer than in breast cancer. Brain metastases are common in patients with lung cancer (30 to 50 %), especially in patients with small cell lung cancer, and also have poor prognosis [47, 48]. A recent Swedish study investigated 17,431 deceased lung cancer patients and confirmed that metastatic sites are influenced by sex, histological subtype, and age at the time of diagnosis. In addition, liver and bone metastases were related to poor survival, compared with nervous system metastases [49]. Increased attention for the early recognition of these extraosseous parenchymal metastases is recommended in cases with vertebral metastases from lung cancer origin compared to breast cancer.

Our study has several limitations. First, the number of patients with prostate cancer was low because of the exclusion of the frequent disseminated involvement of vertebral bodies. Accordingly, it was impossible to calculate the significance levels with the appropriate Chi square test in numerous cases. Second, it must be also taken into consideration that MRI cannot detect lesions under 3 mm and by excluding the micrometastases from the analysis, our results may potentially be biased [50]. Third, vertebral metastases were selected based on their typical MR signal characteristics on T1 and STIR sequences, and no histology was obtained from the vertebrae. The strengths of the investigation include the use of 3T MRI platform with high resolution, and the relatively large number of investigated lung and breast cancer patients.

In summary, we demonstrated significant differences in the skeletal metastatic pattern of common primary tumours using magnetic resonance imaging. These findings may help in the differential diagnosis and have an impact on both patient management and prognosis. In addition, these results may help to establish better diagnostic strategies for patients with metastatic disease of the spine.

Acknowledgments We acknowledge the financial support (travel grant) of GE for ADT and DLT and the help of Peter Mechtler in the language editing.

Funding No funding decrared.

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical approval For this type of study formal consent is not required.

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