Differentiation of Myeloma and Metastatic Cancer in the Spine Using Dynamic Contrast Enhanced MRI

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Purpose:

Myeloma and metastatic cancer are commonly seen malignant cancers in the spine. Their morphological appearance can be very similar on MRI, and difficult to be differentiated. The treatment and prognosis are also different. A correct diagnosis based on imaging would help guiding the biopsy and the subsequent treatment planning and prognosis. Angiogenesis is essential for providing nutrients to support the growth of tumor. Dynamic-contrast enhanced (DCE) MRI is commonly applied to evaluate the perfusion and vascular permeability in various cancers, but there were limited reports studying the cancer of the spine [1-3]. In this study we applied DCE-MRI to characterize multiple myeloma and metastatic cancers of different primary. The qualitative evaluation of the DCE pattern (persistent/plateau or wash-out), quantitative analysis of the enhancement percentage and wash-in/wash-out slope, and pharmacokinetic modeling analysis were applied to obtain the characteristic DCE parameters. ROC analysis was performed to evaluate the performance of DCE-MRI for differential diagnosis.

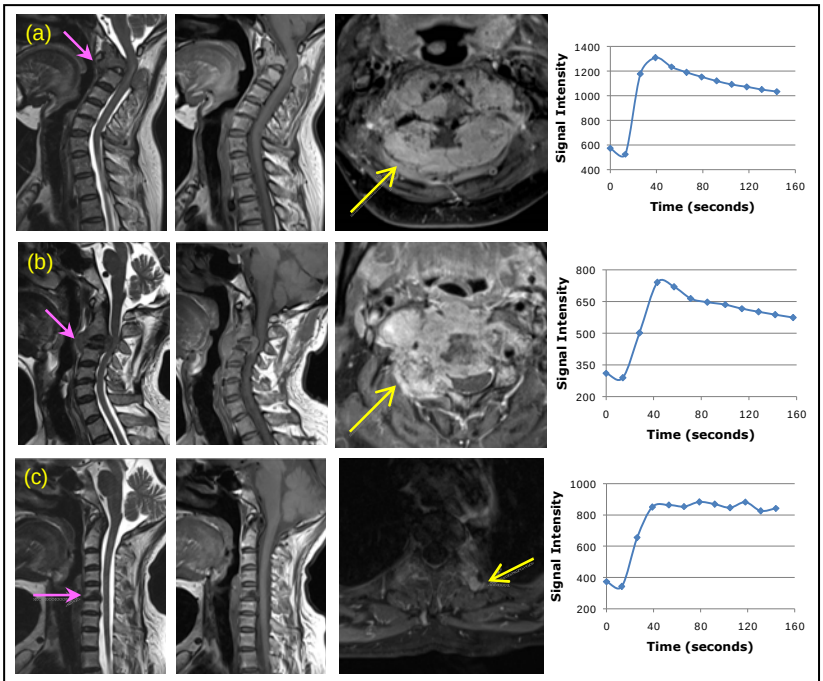

Fig.1: Three case examples. The Sagittal T1, T2, and Axial contrast-enhanced images are shown. The diagnosis cannot be made based on their morphological appearance. (a) A myeloma showing wash-out DCE pattern, Ktrans=0.069/min, kep = 0.96/min; (b) A metastatic thyroid cancer showing wash-pout DCE pattern, Ktrans=0.073/min, kep = 0.90/min; (c) A metastatic breast cancer showing plateau DCE pattern, Ktrans=0.062/min, kep = 0.44/min.

Methods:

Nine patients with myeloma (mean age 58) and 22 patients with metastatic cancer (mean age 55) were analyzed in this study. The MRI scan was performed using a Siemens 3.0T Trio scanner. The pre-contrast T1 and T2 (both fat-suppressed and non-fat-suppressed) weighted images were acquired in Sagittal view to locate the tumor. Then the dynamic contrast-enhanced imaging was performed using a FLASH 3D VIBE sequence. The parameters were: TR= 4.1 ms, TE= 1.5 ms, flip angle= 10°, matrix = 256 x 192, FOV = 250 x 250 mm, and 30 slices (3 mm thickness with 0.6 mm gap) were used to cover the lesion on the axial plane. The temporal resolution varied slightly from 10 to 14 seconds. A total of 12 frames were acquired, so the covered DCE time period was ranging from 120 to 160 seconds. The contrast agent, 0.2 mmol/kg, was injected after one pre-contrast frame was acquired. The ROI was manually placed on the strongly enhanced tumor area. The maximum signal enhancement percentage (SE%) and the SE% in the steepest wash-in segment (determined as the two adjacent time points that show the largest signal increase) were measured. In addition, the two-compartmental pharmacokinetic analysis was applied to obtain the transfer constant (Ktrans) and the rate contrast (kep). The results were compared between the two groups of tumors, and used in ROC analysis.

Results:

Three case examples are illustrated in **Fig. 1**, one myeloma showing the wash-out DCE pattern, one metastatic thyroid cancer showing the wash-out DCE pattern, and another metastatic breast cancer showing the plateau pattern. Myeloma and metastatic cancer groups have significant differences in their DCE pattern: 9/9 myeloma vs. 12/22 metastatsic cancers show wash-out. All analyzed quantitative DCE parameters are listed in **Table 1**. It can be seen that myeloma has significantly higher maximum(peak SE%) and wash-in SE%. Also, for those tumors that showed the wash-out pattern, the mean wash-out slope (between the maximum and the last time points) was 59% for 9 myelomas, and 36% for 12 metastatic cancers. The Ktrans and kep analyzed from the pharmacokinetic modeling analysis showed consistent results, higher in the myeloma group compared to the metastatic cancer group. The mean Ktrans was 0.114/min for myeloma and 0.077/min for metastatic cancer group, and the mean kep is 0.88/min for myeloma and 0.49/min for metastatic cancer group. The ROC analysis was performed to distiguish between these two groups, and the area under the curve was 0.798 for Ktrans, 0.864 for kep, and increased to 0.919 using combined Ktrans and kep, as shown in **Fig. 2**. We also compared the DCE parameters analyzd from metastatic cancers coming from different primary. As shown in **Table 2**, there is no significant difference between any of these tumor subtypes.

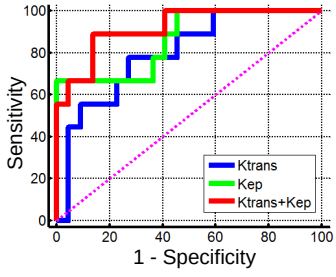

Fig.2: The ROC curves to differentiate myeloma from metastatic cancer. The AUC is 0.798 for Ktrans, 0.864 for kep, and it increases to 0.919 using Ktrans + kep.

Discussion:

Spinal myeloma and metastatic tumor both affect bone marrow, and have similar morphological imaging presentations on conventional MRI, thus cannot be differentiated [4]. In general, it is difficult to differentiate between benign and malignant lesions in the spine, and it is even more difficult to predict the type of tumors. All patients analyzed in this study presented similar pain symptoms, which were suspected to come from compression of spinal cord due to presence of lesions. Compared to metastatic cancer, myeloma had a higher enhancement, faster wash-in and wash-out, and higher Ktrans and kep. The results suggest that myeloma has a higher blood perfusion and vascular permeability that are likely to be associated with a higher angiogenesis. DCE-MRI may provide helpful information for differentiating between myeloma and metastatic cancer. A correct diagnosis based on imaging would help guiding the biopsy and the subsequent treatment planning, which is especially important for patients who do not have a known primary cancer.

Table 1: Quantitative parameters analyzed from DCE kinetic curves of two tumor groups

	Peak SE%	Max Wash-in SE %	Ktrans (1/min)	kep (1/min)
Myeloma (N=9)	226 ± 72 %	169 ± 51 %	0.114 ± 0.036	0.88 ± 0.26
Metastasis (N=22)	165 ± 60 %	111 ± 41 %	0.077 ± 0.028	0.49 ± 0.23
P value	0.044	0.010	0.016	0.002

Table 2: Quantitative DCE parameters analyzed from metastatic cancer of different primary

	Peak SE%	Max Wash-in SE %	Ktrans (1/min)	kep (1/min)
Lung (N=7)	159 ± 43 %	104 ± 27 %	0.075 ± 0.020	0.49 ± 0.23
Thyroid (N=5)	173 ± 45 %	128 ± 44 %	0.083 ± 0.021	0.61 ± 0.29
Liver (N=4)	123 ± 19 %	92 ± 20 %	0.059 ± 0.011	0.44 ± 0.29
Breast (N=3)	206 ± 110 %	143 ± 74 %	0.100 ± 0.052	0.53 ± 0.20
Kidney (N=2)	173 ± 122 %	92 ± 51 %	0.080 ± 0.057	0.54 ± 0.22
Prostate (N=1)	199 %	86 %	0.058	0.58

References: [1] Chen et al. JMRI 2002;15:308-14. [2] Rahmouni et al. Radiology. 2003;229:710-7. [3] Hillengass et al. Clin Cancer Res. 2007;13:475-81. [4] Kim et al. Clin Imaging. 1999; 23:125-133.