Pharmacokinetic Analysis for Differentiating Benign and Malignant Spinal Tumors Measured by DCE-MRI

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Background and Purpose:

Patients presenting pain in the spine who are suspected to have lesions compressing the spinal cord are often recommended to receive MRI for diagnosis. A correct diagnosis of the detected lesions is critical for choosing the subsequent biopsy or treatment procedures. Four different lesions were analyzed in this work, including three malignant (primary myeloma, metastatic cancer, lymphoma) and one benign (tuberculosis) groups. Their morphological appearance can be very similar on MRI, and difficult to be differentiated (see **Fig.1**). Dynamic contrast enhanced (DCE) MRI is commonly applied to evaluate the perfusion and vascular permeability in various tumors, but there were limited reports studying lesions of the spine. Since it is difficult to measure the blood curve from each individual patient, the pharmacokinetic analysis is often performed using assumed blood curves established from healthy population. In this study we applied three different blood curves (fast, medium, and slow) to analyze Ktrans and kep from the DCE kinetics measured from these different lesions to differentiate among them. The obtained fitting parameters were correlated with peak signal enhancement, wash-in slope and wash-out slope directly measured from the DCE kinetics; also the parameters analyzed using different blood curves were compared.

Methods:

A total of 62 patients were analyzed in this study, including 9 patients with myeloma, 22 patients with metastatic cancer, 7 patients with spinal lymphoma, and 24 patients with tuberculosis. 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 lesion. 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 contrast agent, 0.2 mmol/kg, was injected after one pre-contrast frame was acquired. The peak 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. For the cases with peak enhancement occurred within the first 60 seconds after injection, the wash-out slope was calculated using the peak and the signal intensity at the last time point. For cases that did not show peak enhancement within the first 60 second, the slope between the signal intensities at the 67 seconds time point and the last time point was calculated. The DCE pattern was determined as "wash-out" when the slope showed > 10% decrease; as "persistent enhancement" when the slope showed > 10% increase, and "plateau" when the change was smaller than 10%. Two-compartmental pharmacokinetic analysis was applied to obtain Ktrans and kep using three different blood curves (using the same parameters as used in the commercial DCE analysis program Tissue4D®).

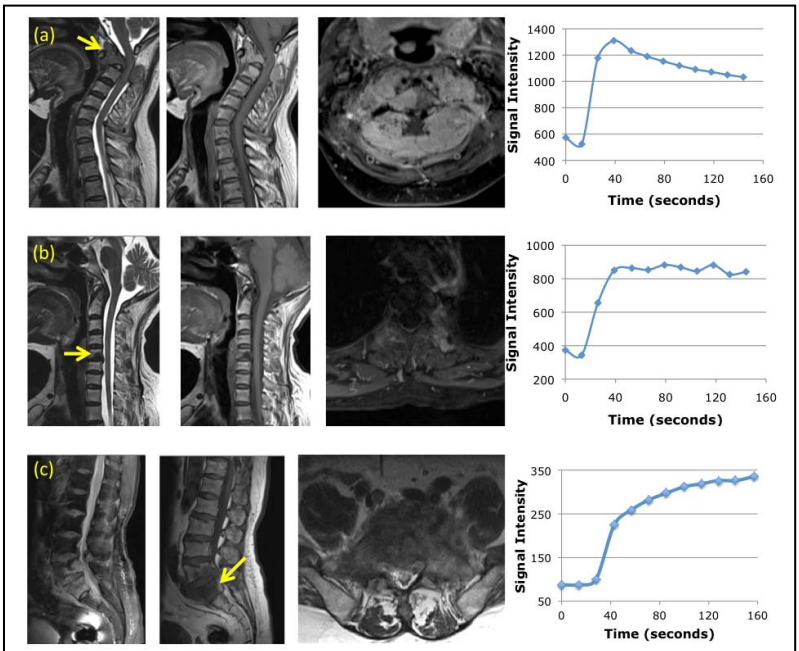

Fig 1. Three case examples. The Sagittal T1, T2, and Axial contrast-enhanced images are shown. (a) A myeloma showing wash-out DCE pattern, Ktrans=0.069/min, kep = 0.96/min; (b) A metastatic breast cancer showing plateau DCE pattern, Ktrans=0.062/min, kep = 0.44/min; (c) A benign tuberculosis showing persistent enhancing pattern, Ktrans=0.086/min, kep = 0.10/min.

Results:

Three cases are illustrated in **Fig. 1**, a myeloma with wash-out, a metastatic breast cancer with plateau, a tuberculosis with persistent enhancing pattern. Comparisons of all analyzed parameters are listed in **Table 1**. Kep analyzed using the fast and medium blood curves are the best parameter to differentiate among these 4 leison groups. **Fig. 2** shows the correlation plot of Peak, wash-in SE%, Ktrans (med), Ktrans(slow) with Ktrans(fast). **Fig. 3** shows the correlation plot of Peak, wash-out SE%, kep(med), kep(slow) with kep(fast). It can be seen that Ktrans and kep analzyed using fast and medium blood curves are highly correlated, but not with those analyzed using the slow blood curve; Ktrans is associated with wash-in and to a lesser extent with peak enhancement; on the other hand, kep is closely associated with wash-out slope and not related to the peak enhancement at all.

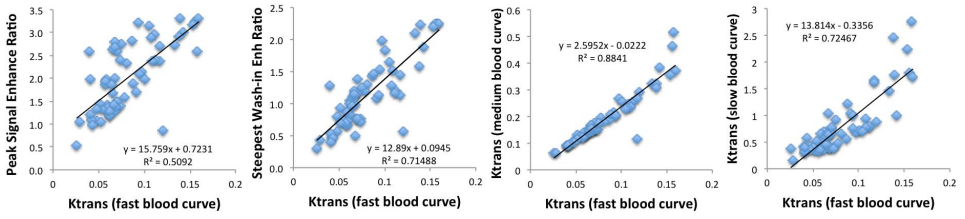

Fig 2. Ktrans(fast) is highly correlated with Ktrans(med), but not with Ktrans(slow). It is moderately correlated with wash-in SE%, and to a lesser extent with Peak SE%. The slow blood curve is not suitable for a short DCE period.

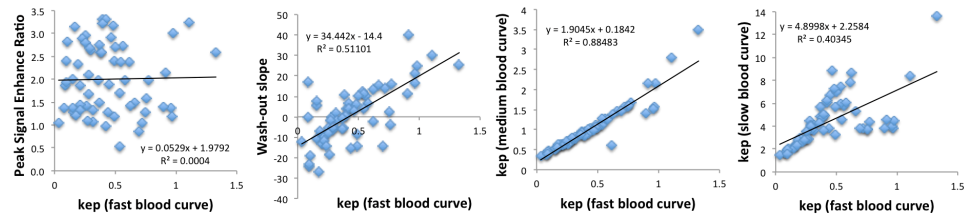

Fig 3. kep(fast) is highly correlated with kep(medium), not with kep(slow). It is correlated with wash-out, not Peak SE%.

Table 1: Quantitative parameters analyzed from DCE kinetic curves of four lesion groups using fast, medium, and slow blood curves

	Peak SE%	Steepest wash-in SE%	Ktrans-fast (1/min)	kep-fast (1/min)	Ktrans-med (1/min)	kep-med (1/min)	Ktrans-slow (1/min)	kep-slow (1/min)
Myeloma (N=9)	226 ± 72 %	169 ± 51 %	0.114±0.036	**0.88 ± 0.26**	0.286±0.146	**1.86 ± 0.88**	1.24 ± 0.77	6.50 ± 3.13
Metastasis (N=22)	165 ± 60 %	111 ± 41 %	0.077±0.028	**0.49 ± 0.23**	0.179±0.068	**1.09 ± 0.39**	0.66 ± 0.32	4.22 ± 1.46
Lymphoma (N=7)	266 ± 37 %	99 ± 30 %	0.068±0.016	**0.34 ± 0.06**	0.155±0.034	**0.83 ± 0.07**	0.67 ± 0.17	4.27 ± 0.79
Tuberculosis(N=24)	204 ± 82 %	101 ± 55 %	0.077±0.036	**0.27 ± 0.15**	0.171±0.083	**0.72 ± 0.25**	0.77 ± 0.63	3.90 ± 2.23

Discussion:

Differentiating benign and malignant lesions in the spine is difficult, and it is even more difficult to predict the type of tumors. A correct imaging diagnosis is critical for the management, and DCE-MRI may provide helpful information. All myeloma showed wash-out and all lymphoma showed plateau pattern; metastatic cancers were heterogeneous; the benign tuberculosis was the most likely to show persistent enhancing pattern. For DCE of approximately 4 min, pharmacokinetic analysis using fast or medium blood curves are suitable, not the slow blood curve.