Application of Two-compartmental Pharmacokinetic Analysis with and without Vascular Term 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 groups of 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. 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 in a clinical setting, the pharmacokinetic analysis is often performed using assumed blood curves established from healthy population. Also, when applying the pharmacokinetic modeling analysis, there was a question of whether the plasma component (vp, or in a more general term "the vascular volume fraction") should be included in the model or not. We have investigated the use of different population–based blood kinetics in the modeling analysis before, and found that the results obtained by using fast and medium blood kinetics were highly correlated. In this study we applied these two different blood curves (fast and medium) to analyze Ktrans and kep, and also compared the results obtained with and without the vascular term to differentiate among the four spinal lesion groups. We hope to gain more understanding about the impact of using different models and blood kinetics on the derived parameters in characterizing different spinal lesions.

Methods:

A total of 125 patients were analyzed in this study, including 9 patients with myeloma, 85 patients with metastatic cancer (from various primary, the most commonly seen lesions in the spine), 7 patients with spinal lymphoma, and 24 patients with benign 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. A total of 12 DCE frames were acquired to cover a total of 120-160 seconds DCE time course. Two-compartmental pharmacokinetic analysis was applied to obtain Ktrans and kep using two different blood curves (fast and medium as used in the commercial DCE analysis program Tissue4D®). The fitting was done by including (with vp) and ignoring the vascular fraction (no vp), and the obtained results were compared. Also, the mean and standard deviation of the derived Ktrans, kep, and the vascular volume fraction for each lesion group was calculated.

Results:

The results of obtained fitting parameters are summarized in **Table 1**. **Figure 1(a) and (b)** show the fitting in one example of myeloma using the fast and medium blood kinetics, respectively. Although the DCE time course shows a rapid wash-in phase, in **Fig 1(b)** there is only a small vascular component. In **Table 1** it is clearly seen that even for the highly vascularized myeloma group the mean vascular volume fraction is only 0.28%. When using the fast blood kinetics, since the vascular [Gd] concentration is very high right after injection, in order to obtain a good fitting quality the vascular volume fraction will be low. **Fig. 1(c) and 1(d)** show the correlation plot of Ktrans and kep obtained with the vp term vs. those obtained without the vp term. It can be seen that since the vascular component is very small, the derived Ktrans are highly correlated, almost all falling on the unity line. For kep, only several cases that have a substantial vp show a decreased kep when considering the vp term. **Figure 2** shows the results obtained using the medium blood curve. Now since the vascular [Gd] concentration is lower, the vascular volume fraction is higher compared to the results obtained using the fast blood curve. The mean vascular volume fraction is 1.8% for myeloma. In **Fig. 2(b)** fitting example, the vascular component is clearly visible. Due to this substantial vascular component for some cases, in **Fig. 2(c) and 2(d)** it can be seen that some cases have a clearly noticeable lower Ktrans and kep when considering the vp component (also see results highlighted in **Table 1**).

Table 1: Quantitative parameters analyzed from DCE kinetic curves for four lesion groups, by using fast and medium blood curves, with and without vascular fraction

	Ktrans- fast no vp (1/min)	Ktrans- fast with vp (1/min)	Vascular fraction-fast (%)	kep- fast no vp (1/min)	kep- fast with vp (1/min)	Ktrans- med no vp (1/min)	Ktrans- med with vp (1/min)	Vascular fraction-med(%)	**kep- med no vp (1/min)**	kep- med with vp (1/min)
Myeloma (N=9)	0.113 ± 0.036	0.109 ± 0.040	0.28 %	0.32 ± 0.13	0.22 ± 0.09	**0.90 ± 0.29**	0.82 ± 0.27	1.8 %	**2.18 ± 0.82**	**1.36 ± 0.35**
Metastasis (N=85)	0.099 ± 0.047	0.099 ± 0.047	0.045 %	0.24 ± 0.12	0.22 ± 0.12	**0.49 ± 0.22**	0.48 ± 0.22	0.8 %	**1.19 ± 0.43**	**1.03 ± 0.36**
Lymphoma (N=7)	0.068 ± 0.016	0.068 ± 0.016	0.0002 %	0.16 ± 0.04	0.15 ± 0.03	**0.34 ± 0.06**	0.34 ± 0.06	0.5 %	**0.91 ± 0.11**	**0.83 ± 0.07**
Tuberculosis(N=24)	0.077 ± 0.036	0.077 ± 0.036	0.027%	0.18 ± 0.08	0.17 ± 0.08	**0.27 ± 0.15**	0.26 ± 0.15	0.6 %	**0.79 ± 0.26**	**0.71 ± 0.25**

Discussion:

In this work we investigated the impact of fitting parameters obtained using a 2-compartmental model with and without considering the vascular volume term. The results obtained using the fast and medium blood curves were compared. Despite a rapid wash-in phase seen in myeloma groups, vascular fraction was still very low. The vascular component could be seen more clearly when a medium blood curve was used, presumably due to its lower [Gd] concentration in the blood. For differentiating among the four different lesion groups, the vascular fraction, Ktrans and kep obtained using the medium blood curve showed significant differences. When the term vp was considered, it had a diagnostic value, but the kep might become less powerful. Satisfactory fitting quality was seen when using all models. These parameters obtained using different models may be combined to find the best diagnostic classifier for differential diagnosis. 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. DCE-MRI may provide helpful information to aid in guiding biopsy or for subsequent treatment planning.

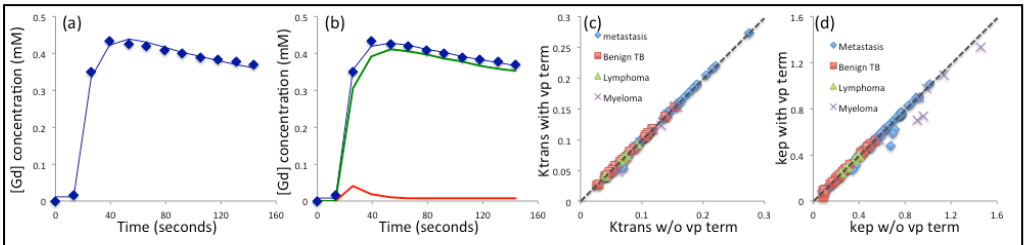

Figure 1. (a) Pharmacokinetic fitting of a myeloma case using the fast blood curve without the vp term; (b) fitting with the vp term (vascular and extra-vascular component shown as the red and green curves). (c) Fitted Ktrans and (d) kep obtained with vs. without vp term. The parameters are highly correlated, mostly falling on the unity line (dashed line).

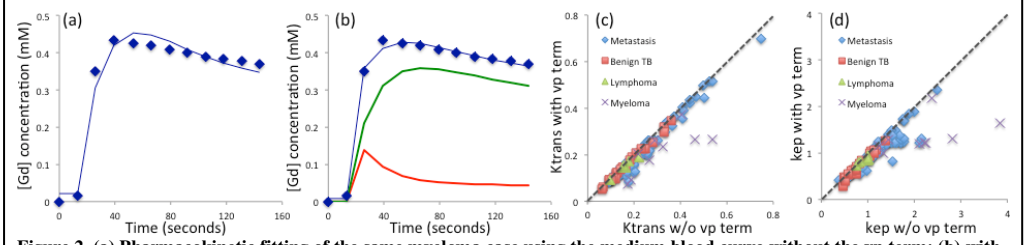

Figure 2. (a) Pharmacokinetic fitting of the same myeloma case using the medium blood curve without the vp term; (b) with the vp term (a higher vascular component is seen compared to Fig.1). (c) Fitted Ktrans and (d) kep obtained with vs. without vp term. Cases with a substantial vascular component have a decreased Ktrans and kep, away from the unity line.