Published in final edited form as:

MAGMA. 2015 December ; 28(6): 555–563. doi:10.1007/s10334-015-0496-1.

Effect of T_2^* correction on contrast kinetic model analysis using a reference tissue arterial input function at 7T

Jin Zhang¹, Melanie Freed¹, Kerryanne Winters¹, and Sungheon G. Kim¹

¹Center for Biomedical Imaging, Department of Radiology, New York University School of Medicine, New York, NY, 10016

Abstract

Object—To investigate the effect of T_2^* correction on estimation of kinetic parameters from T_1 -weighted dynamic contrast enhanced (DCE) MRI data when a reference-tissue arterial input function (AIF) is used.

Materials and Methods—DCE-MRI data were acquired from 7 mice with 4T1 mouse mammary tumors using a double gradient echo sequence at 7T. The AIF was estimated from a region of interest in the muscle. The extended Tofts model was used to estimate pharmacokinetic parameters in the enhancing part of the tumor, with and without T_2^* correction of the lesion and AIF. The parameters estimated with T_2^* correction of both the AIF and lesion time-intensity curve were assumed to be the reference standard.

Results—For the whole population, there was significant difference ($p < 0.05$) in transfer constant (K^{trans}) between T_2^* corrected and not corrected methods, but not in interstitial volume fraction (v_e). Individually, no significant differences were found in K^{trans} and v_e of four and six tumors, respectively, between the T_2^* corrected and not corrected methods. In contrast, K^{trans} was significantly underestimated, if the T_2^* correction was not used, in other tumors of which median K^{trans} was larger than 0.4 min^{-1} .

Conclusion— T_2^* effect on tumors with high K^{trans} may not be negligible in kinetic model analysis, even if AIF is estimated from reference tissue where the concentration of contrast agent is relatively low.

Keywords

DCE-MRI; contrast kinetic model; T_2^* effect; reference tissue; arterial input function

Please send correspondence to: Sungheon G. Kim, PhD, Bernard and Irene Schwartz Center for Biomedical Imaging, Department of Radiology, New York University School of Medicine, 660 First Ave, 4th Floor, New York, NY 10016, Phone: 212-263-2717, Fax: 212-263-7541, Gene.Kim@nyumc.org.

COMPLIANCE WITH ETHICAL STANDARDS

Ethical approval: All mice were treated in strict accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and this study was approved by the Institutional Animal Care and Use Committee.

Informed consent: Not applicable.

Conflict of interest: This study was funded by NIH1R01 CA160620. There is no conflict of interest.

INTRODUCTION

Gadolinium(Gd)-based contrast agents have been used to measure blood volume and flow using T_2^* -weighted dynamic imaging [1] or vascular leakiness and its associated tissue microcirculation properties using T_1 -weighted dynamic imaging [2]. In T_1 -weighted dynamic contrast enhanced magnetic resonance imaging (DCE-MRI), it is typically assumed that T_2^* has a negligible effect on the data. This assumption may be valid in general as most DCE-MRI scan protocols employ minimal echo times around 1–3 ms [3–5]. When the T_2^* effect is negligible, the conversion of time-intensity curves to time-concentration curves is simplified as the signal enhancement depends only on changes in T_1 induced by contrast agent concentration. However, a recent study [6] has demonstrated that the T_2^* effect may not be negligible in practice.

The influence of the T_2^* effect on T_1 -weighted DCE-MRI data can be more pronounced at a high magnetic field strength, such as 7T, as the T_2^* of tissue becomes shorter with the increase of field strength. It has also been recently shown that, even at 3T, which is widely used for routine clinical imaging, the effect of T_2^* cannot be ignored [6]. An arterial input function (AIF) measured from a major vessel could be substantially underestimated due to larger T_2^* effects from higher concentrations of contrast agent. In contrast, the T_2^* effect on a lesion signal intensity curve should be relatively less due to its lower contrast agent concentration compared to that in the plasma. This difference in T_2^* effect between the lesion and plasma results in overestimation of the contrast kinetic model parameters.

The decrease in T_1 -weighted signal intensity due to the T_2^* effect can be corrected by measuring T_2^* using multiple echoes per excitation [7,8]. While this method can directly correct for the T_2^* effect, it results in a lower temporal resolution due to an increased repetition time (TR) and can be more sensitive to noise as T_2^* becomes short. Alternatively, the T_2^* effect on the AIF can be reduced by using two injections of contrast agent at half dose with a sufficient delay in between the injections to keep their peak enhancements well separated [9]. Another possibility is to estimate AIF from a reference tissue, such as muscle [10]. Since the contrast agent concentration in muscle tissue is not as high as in an artery, we expect the T_2^* effect to be smaller for a reference tissue AIF than for a directly measured AIF. However, it has not been shown to date how T_2^* variation following contrast agent injection affects DCE-MRI kinetic model analysis with a reference tissue AIF.

The aims of this study were to investigate the effect of T_2^* changes on 1) the reference tissue AIF estimated from muscle, where Gd concentration remains relatively low, and 2) the contrast kinetic model parameters of tumors when using a reference tissue AIF.

MATERIALS AND METHODS

Animal Model

Six- to eight-week-old BALB/c mice ($n = 7$) were given a subcutaneous injection of 1×10^5 4T1 mouse mammary tumor cells, suspended in 0.1 mL of phosphate-buffered saline, in the right flank. All mice were scanned between post-injection days 10 and 13 when the longest diameter of the tumor was approximately 10 mm. For MRI scans, general anesthesia was

induced by 1.5% isoflurane in air. The animal was mounted on a cradle with respiratory and temperature monitoring probes. The animal body temperature was maintained at $33 \pm 2^\circ\text{C}$ during the scan. All mice were treated in strict accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and this study was approved by the Institutional Animal Care and Use Committee.

Data Acquisition

MRI experiments were performed on a 7T micro-MRI system, consisting of a Biospec Avance II console (Bruker Biospin MRI, Ettlingen, Germany) interfaced to a 200-mm horizontal bore magnet (Magnex Scientific, Yarnton, Kidlington, Oxfordshire, UK) with an actively shielded gradient coil (Bruker, BGA-95; gradient strength, 750 mT/m). A quadrature Litz coil (42mm (length) $\times$ 38mm (diameter), Doty Scientific, Columbia, SC, USA) was used to image the animal while mounted on a cradle with respiratory and temperature monitoring probes.

Before injection of the contrast agent, measurement of T_1 was performed using an inversion recovery pulse sequence with $TR/TE = 12\text{ s}/3.82\text{ ms}$ and inversion times of 0.05, 0.5, 2.5 and 5 s. The dynamic study was performed using a three-dimensional (3D) multiple spoiled gradient echo sequence in steady state with Cartesian K-space sampling and no parallel imaging. Scan parameters were $TR/TE_1/TE_2 = 12/2.593/6.793\text{ ms}$, flip angle (α) = 15° , acquisition matrix = $128 \times 72 \times 9$, reconstructed image matrix = $128 \times 128 \times 9$, resolution = $0.25 \times 0.25 \times 2\text{ mm}^3$, temporal resolution = 7.8 s. The first echo was the shortest echo time allowed in the product sequence. This sequence was run to acquire sixty 3D images in about 8 min. A bolus of 10 mM Gd-DTPA in phosphate buffered saline, corresponding to a dose of 0.2 mmol/kg, was injected through a tail vein catheter 1 min after the start of data acquisition.

Data Analysis

The spoiled gradient echo signal is modeled as the following [11]:

$$S_{TE}(t) = S_0 e^{-TE/T_2^*} \frac{(1 - e^{-R_1(t)TR}) \sin(\alpha)}{1 - \cos(\alpha) e^{-R_1(t)TR}} \quad (1)$$

where S_0 represents the relaxed signal for a 90° pulse when $TR \gg 1/R_1(t)$, α is the flip angle, and $R_1(t)$ is the apparent longitudinal relaxation rate depending on the concentration of contrast agent in the tissue at time t . T_2^* values of individual voxels at each time point were estimated from the double-echo data;

$$T_2^*(t) = (TE_2 - TE_1) / \ln(S_{TE1}(t) / S_{TE2}(t)), \quad (2)$$

where $S_{TE1}(t)$ and $S_{TE2}(t)$ are the spoiled gradient echo signal intensities measured at the two echo times, TE_1 and TE_2 , respectively. We used $S_{TE1}(t)$ as the uncorrected time-intensity curve (TIC) and $S'_{TE1}(t) = S_{TE1}(t) / \exp(-TE_1/T_2^*(t))$ as the T_2^* -corrected TIC as

$$S'_{TE1}(t) = S_0 \frac{(1 - e^{-R_1(t)TR}) \sin(\alpha)}{1 - \cos(\alpha) e^{-R_1(t)TR}} \quad (3)$$

without the T_2^* decay term.

The signal enhancement by contrast agent can be expressed as a ratio between $S_{TE}(t)$ and $S_{TE}(0)$ which eliminates S_0 and the T_2^* decay term, and makes it possible to estimate $R_1(t)$ from the measured data. Indirect estimation of the CR concentration can be made from the estimated $R_1(t)$. We assumed the fast exchange limit and use a linear relationship between the contrast agent concentration $C(t)$ and $R_1(t)$:

$$R_1(t) = R_{10} + r_1 C(t) \quad (4)$$

where R_{10} is the longitudinal relaxation rate of tissue before contrast injection, and r_1 is the contrast agent relaxivity [11].

The AIF was estimated using the muscle as a reference region [10]. The Gd concentration in the plasma, $C_p(t)$, was estimated from either T_2^* corrected or uncorrected data of the reference region tissue, $C_t(t)$, using the following equation [12]:

$$C_p(t) = C_t(t) / v_e + (1/K^{trans}) dC_t(t)/dt \quad (5)$$

where the reference muscle transfer constant, K^{trans} , and interstitial volume fraction, v_e , were assumed to be 0.11 min^{-1} and 0.15 , respectively [10]. In order to minimize the effect of the noise, a multiple layer feed-forward back propagation neural network (2 hidden layers with 2 neurons in each hidden layer) was used to estimate a smoothed tissue concentration curve [13]. The extended Tofts model [14] with a vascular compartment was used for contrast kinetic model analysis to obtain the transfer constant (K^{trans}), interstitial volume fraction (v_e), and vascular plasma volume fraction (v_p). The model was fitted to either T_2^* corrected or uncorrected lesion TIC (LTIC) by minimizing the sum of squares of the difference using the Simplex [15] method provided in Matlab (MathWorks, Natick, MA).

Since T_2^* correction can be applied to the AIF and/or the LTIC, there are four different methods of T_2^* correction included in this study: (I) both AIF and LTIC corrected; (II) no correction; (III) only AIF corrected; (IV) only LTIC corrected. The kinetic parameters estimated using method I were assumed to be the most accurate and were used as the reference standard for comparison with the other T_2^* correction methods. The correction methods III and IV were used to assess how much impact there is by correction of either AIF or LTIC alone. Contrast kinetic model analysis was performed on a voxel-by-voxel basis, unless stated otherwise. Wilcoxon rank sum test was used to assess differences between kinetic parameters estimated in using the different T_2^* correction methods. A paired t -test was used to compare goodness of fit between data from two different correction methods. The effect of AIF T_2^* correction on goodness of fit was assessed to examine whether a poor fit could have affected the comparisons between contrast kinetic parameters from different T_2^* correction methods.

RESULTS

Figure 1a shows an example post-contrast T_1 -weighted image with regions of interest (ROI) indicated for the muscle and the enhancing part of the lesion. The ROIs were selected using a post contrast image. Tumor vessels were not segmented out due to a relatively low spatial resolution of our DCE-MRI protocol. The corresponding T_2^* maps of the same slice in Figure 1a are shown for three different time points (baseline, peak, and washout) in Figure 1b, with zoom in map for tumor ROI is also shown here. It is apparent from Figure 1c, T_2^* values near the peak are shorter than at baseline or washout for the ROIs of the muscle and enhancing portion of the tumor. It is shown in Figure 1c that the T_2^* effect has a higher impact for the lesion (the T_2^* value dropped from about 12 ms at baseline to 6 ms at peak; the equivalent R_2^* change is 83 s^{-1}) than the muscle (about 7 ms at baseline to 5 ms at peak; the equivalent R_2^* change is 57 s^{-1}), which indicates high vascularity and/or vascular leakiness of the lesion [16]. Figure 1d shows $S_{TE1}(t)$ and $S_{TE2}(t)$ of the muscle ROI along with T_2^* -corrected TIC, $S'_{TE1}(t)$.

Figure 1e shows the AIFs estimated from $S_{TE1}(t)$ and $S'_{TE1}(t)$ of the muscle reference region shown in Figure 1d. The corrected AIF cannot be achieved by a linear scaling of non-corrected AIF based on the area under curve or the peak magnitude; they have shape different curve patterns. This demonstrates that T_2^* correction of the muscle signal results in a substantial increase in the estimated AIF. A similar effect has been seen when T_2^* correction is applied directly to the plasma signal [6]. Figure 1f shows example model fits to the T_2^* corrected and uncorrected LTIC.

Representative examples of kinetic model parameter maps are shown in Figure 2a and 2b for the mouse presented in Figure 1. The parameter maps of Method-I (both AIF and LTIC corrected) appear similar to those of Method-II (no correction) more than those of Methods-III and IV. The parameter maps of Method-III (only AIF corrected) show noticeably lower K^{trans} and v_e than those of Method-I and II, whereas Method-IV (only LTIC corrected) maps show higher K^{trans} and v_e values in general than those of Method-I and II. There was no remarkable difference in v_p estimates for the particular case shown in Figure 2. The differences between the K^{trans} values for different correction methods for pixels in the enhancing rim increases as the reference standard (Method-I) K^{trans} increases (Figure 2c). However, the differences correspond to similar percentage changes as shown in the relative error plot (see Figure 2d); median: -19.8% (inter-quartile ranges: -26.4% , -6.0%) for Method-II, -48.8% (-53.0% , -39.0%) for Method-III, and 54.7% (53.1% , 56.1%) for Method-IV. Similar trends are also found for v_e estimates; 10.7% (8.7% , 18.1%) for Method-II, -19.7% (-21.5% , -12.0%) for Method-III, and 38.9% (37.2% , 39.5%) for Method-IV. Since Method-IV analysis uses the same T_2^* corrected LTIC as Method-I, the difference between these two methods reflects the effect of T_2^* correction of the AIF. This appears to consistently shift both K^{trans} and v_e values for all voxels. A similar effect can also be observed in the relative error percentage as shown in Figure 2d and 2f. Methods II and III have similar trends in K^{trans} and v_e values since they both use the same, uncorrected LTIC.

The voxel-wise estimates of K^{trans} , v_e , and v_p values for all 7 animals are summarized in Figure 3 in terms of differences in the values from those of Method I. Overall, results from

Method-II are closest to those of Method-I. Among all 7 animals, only one mouse shows a significant difference in v_e between Method-I and Method-II corrections. Four out of seven animals show no significant difference in K^{trans} between Method-I and Method-II. The large underestimation of K^{trans} values for Mouse 2 and 5 can be explained by the fact that these mice have the highest K^{trans} values (median value: 0.59/min and 0.45/min, respectively) among the 7 animals. The median and interquartile range (25%, 75%) of $K^{trans}/v_e/v_p$ values estimated using Method-I are provided in Table 1. As seen in Figure 2c, T_2^* corrections have a larger influence on data with inherently high K^{trans} values. Among all 7 mice, Method-III corrections resulted in significant under-estimation of K^{trans} and v_e , in tumors in 4 mice. In contrast, Method-IV corrections lead to significant over-estimation of K^{trans} and v_e in tumors of 3 mice and 5 mice, respectively. v_p estimates show similar trends as K^{trans} although the values are quite small.

Figure 4 shows Bland-Altman plots of all tumor voxels pooled from all 7 mice for overall comparison of the different correction methods. Most difference data have a mean difference close to zero and they are within the lines of agreement. However, both Method-II and Method-III data have negative trends; the higher the mean values are, the bigger the degree of underestimation in terms of all three parameters (Figure 4a and 4b). The v_e estimates of Method-II appear to have a less obvious trend (regression line slope is -0.03 compared with -0.24 for Method-III and 0.21 for Method IV). In contrast, Method-IV data show positive trends; the higher the mean values, the larger the degree of overestimation in all three parameters. For the whole voxels pooled from all enhancing tumor regions, there was significant difference ($p < 0.05$) in K^{trans} between T_2^* corrected and not corrected methods, but not in v_e .

The effect of T_2^* correction observed in this study is summarized in Figure 5 using median relative errors in K^{trans} and v_e values from lesions in the individual animals. Method-II parameters are distributed closest to the origin (i.e., Method-I). Method-III parameters are in the lower left quadrant indicating under-estimation of both K^{trans} and v_e , whereas the Method-IV parameters in the upper right quadrant demonstrate over-estimation of both parameters.

Goodness of fit was evaluated with a paired t -test. Method-I was tested against Method-IV and Method-II was tested against Method-III as the same LTIC curves are used in each pair; the LTIC is corrected in Method-I and IV, and not corrected in Method-II and III. Among all 14 comparisons, only one case showed a significant difference in terms of goodness of fit (data not shown). Thus, T_2^* correction of the AIF did not appear to influence the model fit in most cases regardless of whether or not a T_2^* correction was applied to the LTIC.

DISCUSSION

The influence of T_2^* effect on lesion signal intensity and AIF can induce systematic errors in contrast kinetic parameter estimation as previous studies [6,17–20] showed. However, it has not been shown that T_2^* effect on contrast kinetic parameter estimation when a reference tissue approach is used where direct measurement of AIF is not feasible. In this study, we investigated the T_2^* effect in T_1 -weighted DCE-MRI experiments using a double-echo

gradient echo sequence where pharmacokinetic parameter estimation was performed using a reference tissue AIF. The results of our study show that the difference between Method-I (correction in both AIF and LTIC) and Method-II (no correction) is quite small and could be negligible when K^{trans} is small. As shown in Figure 3, four out of five animals with relatively low K^{trans} (median value $< 0.25/\text{min}$) showed no significant differences between Method-I and II. This suggests that T_2^* correction may not be necessary if K^{trans} is small and a reference tissue AIF is used. On the other hand, Mouse 2 and 5, whose median K^{trans} values are relatively high (median value: $0.59/\text{min}$ and $0.45/\text{min}$ respectively) showed significant differences between Method-I and II, which indicates that T_2^* effect is more apparent for higher K^{trans} value.

When T_2^* -correction was used for the AIF, but not for the LTIC (Method-III), the estimated kinetic parameters were lower than those from the case with no correction (Method-II) which is consistent with previous work using the directly measured AIF [6,18]. The estimation error appears to be linearly proportional to K^{trans} as shown in Figure 2c and Figure 4, suggesting that T_2^* correction is more important for lesions with large K^{trans} values. The results of Method-III and Method-IV suggest that T_2^* effect is stronger in the lesion, when K^{trans} is high, than in the reference tissue AIF. In contrast, T_2^* effects on the v_e show a similar amount of changes, in opposite directions, by Method-III (AIF corrected) and Method-IV (LTIC corrected), such that v_e estimates without T_2^* correction (Method-II) do not show any remarkable error.

A previous study by de Bazelaire et al [18] showed underestimations of peak arterial Gd concentration ($>4\text{mM}$) by $59\pm38\%$ among 18 patients due to the T_2^* effect. The underestimations were reduced by correction with T_2^* measurements. De Naeyer et al [21] also showed that neglecting T_2^* could lead to errors in arterial concentration estimation up to 43%. In contrast, the corresponding underestimation of the AIF in our study ranged from 6.2% to 37.1% with a mean of 21.3%, indicating that the T_2^* effect in reference muscle tissue may be smaller than in direct arterial measurements. AIF underestimation resulted in substantial overestimation of K^{trans} by 58% in de Bazelaire et al [18] and about 48% in our current study.

One of the limitations of our study was that the contrast kinetic properties of the muscle ($K^{trans}=0.11/\text{min}$ and $v_e=0.15$) were assumed same for all animals. This assumption may not hold true in reality and could affect the estimation of the lesion contrast kinetic properties. However, the main object of this paper was to evaluate the relative changes in the contrast kinetic parameters due to the T_2^* effect and we assumed that the effect from the variation in the muscle contrast kinetic properties is negligible. Future studies can include assessment of this assumption along with employing more advanced techniques for reference tissue AIF [22,23].

Double gradient echo sequences have also been used in other studies for T_2^* correction [17,24,25]. Multiple gradient echo sequences with more than two echoes may help to improve the T_2^* estimation accuracy further and to also reduce the sensitivity to the selected TE, as shown by Zhuo et al [26], although acquisition of multiple gradient echoes decreases the temporal resolution, which is not favorable for contrast kinetic model analysis in general.

Alternative approaches could be to estimate the AIF from phase measurements [27] or by post processing techniques based on transverse relaxivity of the MR contrast media [21] or shape of the vascular signal [28]. Further study is required to assess the feasibility of applying these techniques to DCE-MRI data analysis using a reference tissue AIF where the T_2^* effect is relatively small as shown in the present study.

One of the limitations of the current study was a small sample size ($n = 7$). Future studies are warranted to investigate the T_2^* effect with a larger cohort as well as in DCE-MRI studies for monitoring tumors undergoing treatment which could induce changes in kinetic model parameters, thus affecting the influence of T_2^* correction. We used only two echoes to estimate T_2^* . More echoes can be used to measure T_2^* more accurately at the cost of increased sampling interval which can also affect the estimation of kinetic parameters. The optimal selection of the number of echoes and sampling period needs to be investigated in future studies. Another limitation of this study was lack of comparison with the directly measured AIF as it is not trivial to measure the AIF directly from an artery in mouse MRI due to the limited spatial resolution. A comparison of the T_2^* effect on a directly measured AIF versus a reference tissue AIF in the same subjects would provide useful insight into the role of a reference tissue AIF for reducing the effect of T_2^* in DCE-MRI studies.

It is not straightforward to generalize the findings in our study to other magnetic field strengths. Since T_2^* typically decreases with increase in the magnetic field strength, the degree of T_2^* effect on DCE-MRI can also be varied depending on the magnetic field strength. However, we expect that the general trend will be similar; T_2^* effect on tumors with high K^{trans} may not be negligible even if AIF is estimated from a reference tissue. This needs to be further investigated in future studies using different magnetic field strengths.

In this study, we investigated T_2^* effect on estimation of contrast kinetic model parameters using in-vivo mouse DCE-MRI data. While such experimental data provide an opportunity to observe the realistic effect of T_2^* in a given experimental condition, it is also noted that there are shortcomings including lack of ground truths, limited range of parameters, and limited flexibility to assess the association with the scan protocol. These limitations can be overcome in a numerical simulation study in which a wider range of parameters and scan protocols based on the literature can be used. A future study is warranted to provide better understanding of the T_2^* effect in DCE-MRI in general.

CONCLUSION

In this study, we investigated the effect of T_2^* -correction of both reference tissue AIF and lesion signal intensity curve on contrast kinetic parameter estimation. Our results suggest that T_2^* effect on tumors with high K^{trans} may not be negligible in kinetic model analysis, even if the AIF is estimated from a reference tissue where the concentration of contrast agent is relatively low. On the other hand, when K^{trans} is small, it has been shown that T_2^* correction may not be necessary if a reference tissue AIF is used.

Acknowledgments

Grant support: National Institutes of Health R01CA160620

The authors would like to thank the New York University High Performance Computing center for their support to conduct in vivo data analysis presented in this study. This study was supported by NIH 1R01 CA160620.

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Figure 1.

Representative case demonstrating T_2^* correction using double gradient echo data. (a) Axial slice with ROIs for reference muscle (white) and enhancing lesion rim (red). (b) T_2^* maps estimated at different times; baseline (30s post injection), near-peak (100s) and washout (400s), red and white ROIs are the same as (a). (c) Average T_2^* curves from the muscle (blue) and lesion (black). (d) Average signal intensity curves from the muscle; thin solid line for echo 1, thin dashed line for echo 2 and thick solid line for T_2^* corrected echo 1 data. (e) AIF generated from corrected echo-1 data (thick red solid) and uncorrected echo-1 data (thin red solid) from the reference region. (f) Lesion enhancement curves from echo 1 (thin black solid), echo 2 (thin black dash) and T_2^* corrected echo 1 (thick black solid), and the corresponding model fit for echo 1 (thin green solid) and corrected echo 1 (thick green solid).

Figure 2.

Estimated kinetic parameters for a representative mouse. (a) K^{trans} , v_e and v_p parameter color maps from Method-I T_2^* correction (white bounding box indicating zoom in area with enhancing lesion rim). (b) Zoom of the parameter color maps for the lesion for all T_2^* correction methods (ROI in red indicating selected lesion enhancing rim as in Figure 1a). Comparison of voxel-wise parameter estimates for K^{trans} (c) and v_e (e) for the enhancing rim as shown in (b). Data are arranged in ascending order of the Method-I parameter. Relative error differences with respect to the Method-I parameters are shown in percentage for K^{trans} (d) and v_e (f). Circles, Method-I (reference standard); asterisks, Method-II; pluses, Method-III; crosses, Method-IV.

Figure 3.

Comparison of contrast kinetic model parameters for the four T_2^* correction methods for all the 7 animals. The box plots show the median and interquartile range (25%–75%) of absolute errors from the lesions for (a) K^{trans} , (b) v_e , and (c) v_p . Green for Method-II, blue for Method-III and red for Method-IV. Wilcoxon rank sum test results were performed to test the difference between parameter absolute value estimated from Method-II, III, or IV and those from Method-I. Significant differences were marked with asterisks on top of each boxplot.

Figure 4.

Bland-Altman plot showing a voxel-wise comparison between Method-I and Method-II (a), Method-III (b) and Method-IV (c) for estimated K^{trans} , v_e and v_p values for all tumor voxels pooled from all 7 animals. Solid thin lines are mean difference (actual values are noted in each plot) and dash thin lines are mean $\pm 1.96SD$. Blue dash lines are regression lines.

Figure 5.

Using median relative percentage error of the estimated K^{trans} on x axis and median relative percentage error of the estimated v_e on y axis, this scatter plot summarizes the distribution of median relative errors for all seven animals by considering K^{trans} and v_e together. Method-I, II, III and IV results are shown as black circles, green asterisks, blue pluses and red crosses, respectively.

Table 1

Contrast kinetic model parameters estimated using Method-I (T_2^* correction on both AIF and LTIC). Included are the median and interquartile range (25%, 75%) for each animal.

Mouse	K^{trans} (/min)	v_e	v_p
<i>1</i>	0.23 (0.09, 0.39)	0.30 (0.24, 0.36)	0.00 (0.00, 0.00)
<i>2</i>	0.59 (0.26, 1.55)	0.39 (0.30, 0.78)	0.03 (0.01, 0.05)
<i>3</i>	0.23 (0.14, 0.42)	0.21 (0.13, 0.48)	0.01 (0.00, 0.01)
<i>4</i>	0.10 (0.06, 0.15)	0.28 (0.18, 1.00)	0.06 (0.02, 0.15)
<i>5</i>	0.45 (0.23, 0.75)	0.22 (0.15, 0.31)	0.00 (0.00, 0.02)
<i>6</i>	0.12 (0.08, 0.20)	0.25 (0.18, 0.40)	0.00 (0.00, 0.01)
<i>7</i>	0.15 (0.10, 0.21)	0.48 (0.32, 0.74)	0.01 (0.09, 0.02)