Dependence of Breast Pharmacokinetic Parameters on pre-contrast T1 and flip angle

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Synopsis

Pharmacokinetic (PK) models have been used to estimate physiological parameters such as permeability and dispersion of the contrast agent and is estimated using the acquired signal, pre-contrast T10, and the acquisition flip angle. In this work, we have determined the dependence of the dispersion models' and Tofts models' PK parameters on T10 and B1 maps, as well as the errors introduced by using constant T10 and B1 values in 11 biopsy-proven tumors. Our results show that PK parameters such as kep of Tofts model and kappa of mLDRW dispersion model are less dependent on T10 and B1 and could potentially be used with higher accuracy and precision even when T10 and B1 maps are not acquired.

Introduction

Pharmacokinetic (PK) models have been used to estimate physiological parameters such as permeability [1] and dispersion [2] of the contrast agent from the temporal changes in gadolinium concentration. The contrast agent concentration can be estimated using the RF-spoiled gradient echo signal, pre-contrast T_{10}, and the acquisition flip angle. However, many datasets are acquired without T_{10} and B_1 map due to longer acquisition duration. Several simulation studies [3] have shown significant errors in K^{trans} and v_e values of Tofts model due to their dependence on T_{10} and B_1, assuming that the model perfectly describes the acquired data. The purpose of this study is to determine the dependence of the dispersion models' [2] and Tofts models' PK parameters on T_{10} and B_1 values, as well as the errors introduced by using constant T_{10} and B_1 values using acquired patient data.

Methods

Figure 1 shows the variation in concentration-time curves introduced by different choice of T_{10} and B_1 for the same signal-time curve. The effect of errors in T_{10} and B_1 values on the PK parameters was studied in 6 patients with 11 biopsy-proven tumors (7 malignant, 6 in the right breast). 3D RF-spoiled gradient echo fat-water separated DCE images were acquired using DISCO [4], a pseudorandom ky-kz sampling scheme enabling a favorable tradeoff between temporal and spatial resolution, on a 3T scanner (GE Healthcare, Waukesha, WI). One pre-contrast and four post-contrast images were acquired with high spatial resolution of 0.5×0.6×1.0 mm and low temporal resolution of 2 min. Fourteen images were acquired during the wash-in period with high temporal resolution of 13s and lower spatial resolution of 0.5×1.2×2.0 mm. Prior to the acquisition of pre-contrast DCE images (FA=12°), 3D variable flip angle (FA=2°, 5° and 8°) images with identical imaging parameters were acquired to estimate the water-only T_{10} map [5]. A 2D multi-slice Bloch-Siegart B_1 map [6] was also acquired with a low spatial resolution of 5×5×5 mm and was also used for correcting the T_{10} map. The DCE images, T_{10} and B_1 maps were subsequently reconstructed to identical spatial resolution of 0.5×1.2×2.0 mm.

Voxel-by-voxel PK mapping was performed using a standard Tofts model [1] with modified Fritz-Hansen arterial input function as well as modified local density random walk (mLDRW) Dispersion model [2]. The PK parameters were estimated for 11 tumors using the following combinations of T_{10} and B_1: (1) T_{10} map, B_1 map, (2) T_{10} map, FA=[0.6 to 1.4]×12°, (3) B_1 map, T_{10}=[1000 to 2000] ms, (4) T_{10}=1500ms, FA=[0.6 to 1.4]×12°, and (5) FA=12°, T_{10}=[1000 to 2000] ms. The PK parameters estimated over the tumor ROI using the T_{10} and B_1 maps was considered as the standard. Every other PK parameter value was compared to the standard using the concordance correlation coefficient (ρ_c).

Results

The median of the B_1-corrected T_{10} within the tumor ROI varied between 1116 ms and 1821 ms and the median relative FA varied between 0.7 and 1.3. Figure 2 shows the box plot of ρ_c for different combinations of T_{10} and B_1 values. Both kep of Tofts model and kappa of mLDRW dispersion model have a higher ρc and lower relative variation. The median and the range of ρ_c for each of the PK parameters for few combinations of T_{10} and B_1 are tabulated in Figure 3. Parameters such as beta and mu have a lower ρc as well as huge variation indicating their sensitivity to T_{10} and B_1 map. These results show that it may be possible to create PK parameter maps without acquiring T_{10} and B_1 maps and using an average value instead. However only few parameters such as k_{ep} and kappa will have relatively high accuracy and precision, and parameters such as beta will have lower precision.

Discussion

The data analysis assumed that the acquired T_{10} and B_1 maps were accurate and the ρ_c was calculated with the maps derived PK values as the standard. However, both T_1 and B_1 mapping introduces errors. The results also show that ρ_c is high when the average value of T_1 and B_1 maps are used and this, or the use of low-pass-filtered maps, may reduce error propagation.

Conclusion

Pharmacokinetic parameters such as k_{ep} of Tofts model and kappa of mLDRW dispersion model are less dependent on T_{10} and B_1 and hence these PK maps could potentially be used clinically with higher accuracy and precision even when T_{10} and B_1 maps are not acquired.

Acknowledgements

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References

[1] Tofts P, et al., JMRI 1999;10:223-232

[2] Mischi M, et al., IEEE EMBS, 2013

[3] Giovanni PD, et al., Phy. Med. Biol. 2010;55:121-132

[4] Saranathan M, et al., JMRI 2014;40(6):1392-1399

[5] Deoni SC, et al., MRM 2003; 49(3):515-526

[6] Sacolick L, et al., MRM 2010; 63(5):1315-1322

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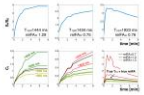
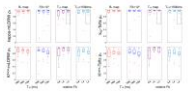
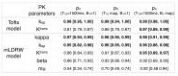
Figures



Dependence of concentration-time curves on T_{10} and B_1. The C_t-time curves corresponding to true T_{10} and true relative FA (relFA) are shown in black. The C_t-time curves are scaled non-linearly with varying T_{10} and B_1.



Both kappa-mLDRW and k_{ep}-Tofts show a lower dependence on T_{10} and B_1 than K^{trans}-mLDRW and K^{trans}-Tofts. The outlier in the kappa-mLDRW and k_{ep}-Tofts corresponds to an average T_{10}=1700 ms and B_1=1.2 and ρ_c is improved with increasing B_1 (gray dashed rectangle)



Concordance correlation coefficient (ρ_c median [25th percentile, 75th percentile]) between the standard PK values estimated with (T_{10} map, B_1 map), and (T_{10}=1500ms, B_1=1), (T_{10} map, B_1=1) and (T_{10}=1500ms, B_1 map). The ρ_c values for Tofts' k_{ep} and mLDRW's kappa are higher showing the least dependence on T_{10} and B_1 values. However, the variation increases for parameters such as beta and mu, showing their dependence on T_{10} and B_1 maps