Sources of errors in pharmacokinetic analysis of DCE-MRI

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INTRODUCTION: Dynamic Contrast Enhanced MRI (DCE-MRI) is a functional imaging method whose use in oncology shows a high potential in assessing and predicting treatment response. Before it can be used in standard clinical oncology, however, it first must be validated with respect to accuracy and reliability. One of the steps required to obtain localized quantitative PK information of tumors is the estimation of the pre-contrast relaxation time, T10. To estimate this parameter, a contrast free sequence of spoiled gradient recalled echo (SPGR) with variable flip angles is used1. Although the effects of incorrect T10 on the computation of PK parameters have already been reported2, motion between the flip angle volumes is still an unexplored problem which may be a relevant source of T10 estimation errors. In rectal tumor scans, for example, deformations are unavoidable, as, in addition to the patient’s movement during the acquisitions, it is also subject to physiological motion and deformation of the organs.

This work aims to evaluate the effects of motion within the variable flip angle sequence on accuracy of the estimation of T10 and in subsequent Tofts3 model PK parameter (Ktrans and kep) estimation. Moreover, we also estimate the amount of motion present in rectal SPGR sequences. Evaluating and correcting potential sources of error in PK analysis by DCE-MRI may improve reproducibility of this procedure and increase confidence in the results from the clinical research being currently performed.

METHODS: Signal intensity (S) in T1 MRI images is a function of the relaxation time (T1), while relaxation time is affected by the contrast agent (CA) concentration.

\[ S = M_0 \sin(\alpha) \left[ 1 - \exp\left(-\frac{TR}{T_1}\right) \right] \]

\[ \frac{1}{T_1} = \frac{1}{T_{10}} + r_1 C \]

These relations are expressed by the following equations:

where M0 is the magnetization, and TR and α are, respectively, the acquisition parameters of repetition time and flip angle. T10 is the contrast free relaxation time, r1 is the CA’s relaxivity constant and C is the CA concentration.

PK analysis by the Tofts model requires the concentration curve over time to estimate perfusion parameters (Ktrans and kep). Thus, to extract this information from DCE-MRI volumes, the CA free relaxation time (T10) needs to be estimated. This may be done by acquiring several SPGR volumes with fixed TR and variable flip angle. Using Eq. 1, for each voxel, a linear regression between the signal intensity of each volume can be performed and T10 and M0 can be estimated1. This approach assumes physical correspondence between the voxels in these volumes, which may not be true if there is motion between these volumes. This motion can lead to misalignment and consequently inaccurate T10 computation, which could then compromise the PK analysis of the DCE-MRI time intensity curves.

In this work we performed tests to: (a) estimate the T10 error when motion is present in variable flip angle MRI sequences; (b) evaluate how this error propagates to Ktrans and kep estimation; (c) quantify the amount of motion found in rectal SPGR variable flip angle sequences.

Estimating T10 error caused by motion: 21 synthetic T10 and M0 volume map pairs were generated from rectal MRI volumes with a mean resolution (in mm3 per voxel) of 0.88x0.88x4.65. These maps were used to generate synthetic variable flip angle SPGR sequences using Eq. 1. For each pair, a sequence of 3 or 4 SPGR volumes with flip angles 3°, 9°, 12° and/or 15° and TR=4.5ms was computed. Random (but known) B-Splines free-form deformations were applied to each of these volumes with different levels of mean displacement. The motion corrupted sequences were then used to estimate T10 and the results were compared with the ground truth data and the mean absolute percentage error was computed (Fig. 1).

Estimating PK parameter error from T10 error: CA curves were generated using the Tofts model and the Orton Arterial Input Function5 for Ktrans values ranging from 0.01 to 2.00 and kep values from 0.01 to 5.00. These curves were then converted into DCE-MRI sequence data using a ground truth T10 (1.0s), as well as TR=4.5ms and TE=2.2ms. These synthetic DCE-MRI curves (S(t)) were then used to estimate the process of estimating Ktrans and kep with inaccurate relaxation time (T10). Iteratively, Ktrans and kep parameters were tested by generating a time intensity curve, which in turn was transformed into a DCE-MRI intensity curve (S*(t)) using Eq. 1 and 2 with T10, Ktrans, and kep parameters for different degrees of T10 deviation (Fig. 2).

CONCLUSION: This work has investigated the sources of error in PK analysis in rectal cancer DCE-MRI. These in particular stem from inaccuracies of T10 estimation in case of motion within variable flip angle sequences, with T10 estimation errors propagating and amplifying subsequent PK parameter estimations (Ktrans and kep). It was demonstrated that even for the average motion (0.43mm) found within these volumes, this may cause more than 15% error in Ktrans and that higher degrees of motion (of up to 0.90mm) may be present. Consequently, care should be taken to account for this source of error in PK parameter analysis.


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