Effects of reference tissue AIF derived from low temporal resolution DCE-MRI data on pharmacokinetic parameter estimation

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Introduction: Quantitative pharmacokinetic analysis of dynamic contrast-enhanced (DCE) MRI data requires knowledge of the arterial input function (AIF). The AIF can be determined from a major artery, a pre-defined 'population' function, or a reference tissue. Direct measurement in an artery is subject to significant systematic errors due to the high contrast media concentration level at early times after injection and partial volume effects. The 'population' AIF does not account for significant variability between patients and contrast media injection protocols. The reference tissue method uses the contrast media concentration curve from a reference tissue, such as muscle, to derive the AIF. A complicating factor for analysis of diagnostic/screening DCE-MRI of the breast is that data is often acquired with low temporal resolution to enable high-spatial resolution coverage of both breasts. Therefore, for both direct measurement and reference tissue AIF estimation, the 'true' AIF cannot be accurately derived and this will affect pharmacokinetic parameter estimation. In this research, we investigated the effect of AIFs derived from reference tissue for a range of temporal resolutions on pharmacokinetic parameter estimation in pre-clinical data.

Method: Pre-clinical DCE-MRI experiments were performed at 4.7 T (Bruker, Billerica, MA, USA) on Copenhagen rats (n = 6) with implanted AT6.1 prostate tumors on the hind limb. Contrast media (Gd-DTPA, dose = 0.2 mmol/kg) was injected at ~30 s after the beginning of the T_1-w GRE acquisition (TR/TE = 40/3.5 ms, flip angle = 30°, FOV = 4 cm, array size = 128^2, linear phase-encoding, 5 s temporal resolution). Data acquisition continued for 10 minutes after injection. The 5-s high temporal resolution DCE-MRI data were downsampled to low (15-s to 85-s) temporal resolutions by applying a k-space-based recombination method [1]. The AIFs were derived from the contrast media concentration curves in muscle [2] using literature values of K^{trans}(= 0.11 min^{-1}) and v_e(= 0.20). The basic Tofts two-compartment model [3] was fit on the mean contrast media concentration curve extracted from the tumor rim, as well as in a pixel-wise manner to estimate K^{trans} and v_e.

Results: Fig. 1 shows the estimated K^{trans} and v_e in tumor rim (averaged over 6 cases) for different temporal resolutions. Surprisingly, errors in K^{trans} and v_e (with respect to parameter values derived at 5-s resolution) were small for 15-s to 60-s resolution data (< 5%). However, the errors can increase to more than 20% at 85-s resolution, in part due to instability of the reference tissue method at this resolution. Fig. 2 shows K^{trans} (left column) and v_e (right column) maps for a typical case at 5-, 30-, 60-, and 85-s resolution. The maps look very similar across temporal resolutions, which is especially true for small K^{trans} regions such as in muscle.

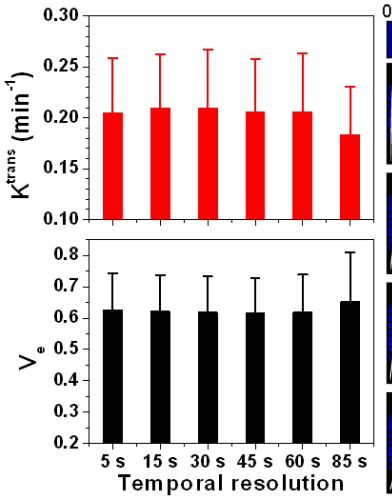

Figure 1.

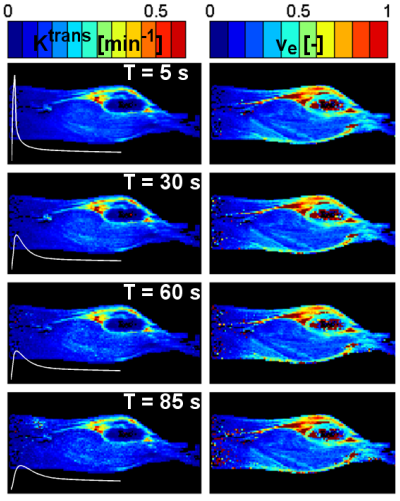

Figure 2.

Discussion: The results demonstrate that the use of AIFs derived with the reference tissue method from low temporal resolution (till T ≈ 60 s) DCE-MRI data leads to unexpectedly small errors. Likely this is due to the use of a slowly enhancing reference tissue, which can be sampled more slowly than the bolus passage in an artery. Because the tissue properties K^{trans} and v_e are expected to be comparable in rats and humans, while blood circulation in rats is faster, we expect that clinical DCE-MRI data of the breast (T ≈ 60 s) could be analyzed quantitatively to estimate K^{trans} and v_e within reasonable error margins. However, similar studies should be performed with clinical data. In this research, the contrast media arrival time was estimated from the 5-s resolution data; in reality, this would have to be estimated from low temporal resolution data. We conclude that the use of an AIF extracted from low temporal resolution data is feasible, but the stability and timing aspects require further investigation.

Reference: [1] Heisen et al., MRM 2009 (in press); [2] Fan et al., MRM 2004; [3] Tofts et al., JMRI 1999.