Bolus Arrival Time extraction using Super Temporal Resolution Analysis of DCE

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Target Audience:

Scientists and clinicians with an interest in perfusion imaging and signal processing algorithms.

Purpose:

DCE is usually acquired using bolus injection and with a temporal resolution of ~6 sec. The commonly used Extended Tofts Model[1] (ETM) disregards inter tissue differences in bolus arrival time (BAT), which are in the order of 1-2 sec [2]. This delay can result from differences in flow in different brain areas due to normal or pathological vasculature, and is an important clinical parameter in several brain vascular pathologies. This study aims to estimate the BAT using a super temporal resolution (STR) analysis, i.e. temporal resolution higher than the acquired one. The proposed method uses ETM with blind estimation of the arterial input function (AIF) (similar to [1]), to extract the BAT, accounting for differences in the local AIF[3]. The method was tested on simulated data, real data obtained from 3 patients with brain tumors, and by comparing DCE-BAT with time-to-peak (TTP) value obtained from DSC.

Methods:

STR-DCE: The proposed method is an extension of the ETM, taking into account the BAT by modeling plasma to tissue concentration as: $\boldsymbol{C(t) = v_p C_p(t') + k^{trans} e^{(-k_{ep} \cdot t)} * C_p(t')}$, where $*$ stands for convolution and $\boldsymbol{t' = t - BAT}$. Individual subject's AIF is extracted using blind estimation[4], while accounting for BAT. The method fits the AIF with several time-shifts (given in a functional form[5], shifted in steps of 0.5sec). For each voxel, the time shift of the best fit is set to be the BAT value in that voxel.

Simulation: A realistic AIF was defined using blind estimation on a set of ten manually marked arterial voxels of a patient with glioblastoma (GB). This AIF was marked as the "true" AIF and was used to simulate a full 4D data using the ETM with pharmacokinetic parameters taken from the patient.

A Gaussian noise (σ =10%) and a random delay taken from the uniform distribution in the [-0.5, 0.5] sec interval were added.

Real Data: All DCE data was acquired on a 3T MRI system. *Comparison to High Temporal Resolution (HTR):* One patient was scanned once with HTR-DCE of ~2 sec; *Comparison to DSC:* Two patients were scanned with DCE using temporal resolution of ~6sec and DSC with temporal resolution of 1.3sec; *Longitudinal scan:* One patient was scanned longitudinally before and two weeks following bevacizumab therapy using DCE with temporal resolution of ~6sec.

Validation of the method using HTR data: The HTR-DCE data was analyzed twice utilizing the proposed method: using the full data, and using a temporal sub-sampling of the data to match the standard temporal resolution. The BAT values were compared between the two analyses.

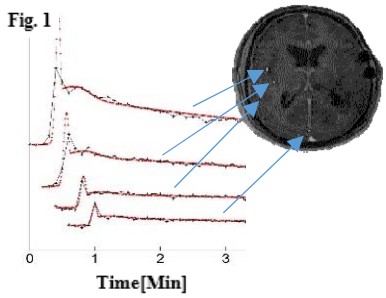
Comparison with DSC: DSC maps were calculated using the Penguin software[6] and TTP maps were compared to the BAT maps, acquired from the standard temporal resolution DCE. Since DSC acquisition has lower spatial resolution, the BAT maps were smoothed before comparison. Pearson correlation between the TTP and the BAT maps were calculated for the two patients.

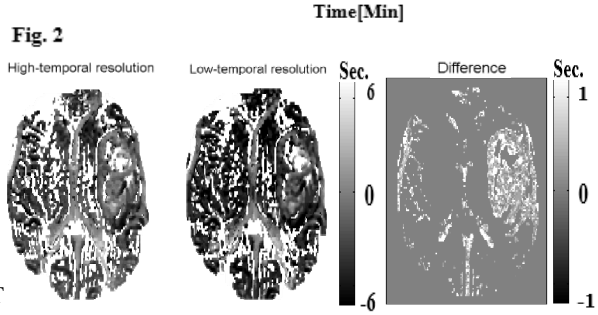
Results and Discussion:

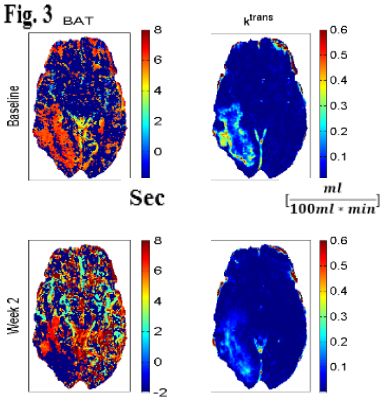
Simulation results: Blind AIF estimation without accounting for BAT resulted in an inaccurate shape and amplitude at peak. Fig. 1 shows example of 4 (out of 10) concentration-time-curves (CTCs, in black), along with fitted parametric CTCs (in red) using the extracted AIF. Note that when allowing a small time-shift for each voxel, the extracted AIF fits well these 4 CTCs. The proposed method enabled extraction of the BAT in all voxels of the simulated 4D data. High correlation was obtained between the original ("true") values used for simulation and the extracted values ($r > 0.92$, $p < 1e\text{-}10$).

Real Data results*: HTR data:* BAT maps estimated from the HTR and sub-sampled DCE data and the difference between them are shown in Fig. 2. A strong significant correlation was found along the whole BAT range (r=0.85, p<1e-10) between the two maps. The median BAT difference was 0.53 sec, and 75% of all voxels in the BAT map estimated from the sub-sampled data showed less than 1sec inaccuracy compared to the HTR data, including most of the voxels within the lesion. The proposed analysis succeeded in capturing the spatial distribution of BAT values in the lesion area. *Comparison with DSC:* Medium and significant correlations between the DCE-BAT and DSC-TTP maps were found (r=0.39, r=0.30, p<0.01 for both). Note that high correlation is neither expected nor desirable, as the two measurements differ in meaning.

Longitudinal patient data: BAT and K^{trans} maps of a patient with GB, scanned before and two weeks after bevacizumab therapy, obtained using a ~6sec temporal resolution DCE are shown in Fig. 3. As expected, treatment effects can be seen by reduction in vessel permeability (K^{trans}). Furthermore, changes in BAT values were detected two weeks following therapy.







Conclusion:

This study shows that accounting for delay in DCE analysis can result in a better estimation of the AIF and provide an additional pharmacokinetic parameter (BAT) relating to the tissue's vasculature, as typical in DSC analysis (TTP). This parameter may have clinical importance in the assessment of patients with vascular diseases.

References: [1] Tofts et al., MRM 1999[2] Artzi et al.Neuroscience 2013 [3] Fluckinger et al., MRM 2010 [4]Fluckinger et al., MRM 2009; [5]Parker et al. ,MRM 2006 ; [6]Østergaard et al., MRM 1996