Highly Accelerated DCE-MRI Pharmacokinetic map Estimation through frequency domain based Tofts model (HAET)

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Target audience: The current study is relevant to those MR researchers interested in DCE-MRI methods and applications, cancer imaging. **Introduction:** Quantitative DCE-MRI is a widely used method for prognosis of cancer. Tofts Model (TM) [1] is an extensively used method for determination of Pharmacokinetics (PK). Curve fitting of concentration time curves (CTCs) for multiple voxels is required for determination of PK maps, which requires long computational time thereby restricting online access to these maps for the radiologist. Hence, there is a need for obtaining PK maps in significantly shorter time. Purpose of this study is to demonstrate a frequency domain (FD) approach in place of existing time domain (TD) approach in order to speed up computational time. **Theory:** The equation for TM in TD is given by $C(t) = K^{trans} e^{(-K_{ep}t)} * C_a(t)$ (1). where C(t) is the concentration of Contrast Agent (CA), $C_a(t)$ denotes Arterial Input Function (AIF) in mM and * denotes convolution operation. The current study solves equation (1) using FD approach and it can be written as in ref [2] as: $real(F^{-1}\{K\}) = real\{K^{trans} E(-K_{ep}t)\}$ (2), Here, K= (K1/K2) where, K_1=F{C(t)} and K_2=F {C_a(t)} and F here denotes FFT operation while F^{-1} denotes inverse FFT operation. **Methods and Materials:** *Simulation data:* CTCs were simulated to assess the current FD approach. All the curves were generated with relative K^{trans} and Ve of 0.0090~0.14 min^{-1} and 0.066~0.55 respectively taken form literature [3], as the Ground Truth (GT) for the evaluation of demonstrated approaches. Average population AIF was used with 28 time points and the CTCs was fit for two parameters (K^{trans} and Ve) using TM in TD and TM in FD, which was considered as Estimated Value (EV). The error between the EV and GT value was determined for the PK maps for both approaches through Normalized Root Mean Square Error (NRMSE). *In-vivo data:* 7 breast DCE data were downloaded from Quantitative Imaging Network (QIN) [4]. Imaging parameters of the data sets were: TR/TE=6.2 ms/2.9ms, temporal resolution 18~20 seconds. Number of time points varied from 28~32 frames in each data sets. The CA used was Gd (HP-DO3A) [ProHance] IV with a dosage of 0.1mmol/Kg at 2 ml/s. Tumor Region Of Interest (ROI) is shown for each data set in yellow outline. CTCs for those ROI pixels were curve fitted for two parameters using both approaches given in equations 1 and 2. Trust-region algorithm was used for curve fitting. The system configuration used to carry out curve fitting was Intel core i5, 2.60 GHz, 4GB RAM and computations were performed using Matlab, Mathworks Inc., Boston, MA. **Performance evaluation:** 7 datasets were evaluated for computational time taken for obtaining PK maps using TM-TD and TM-FD approach. Computational time taken for estimating PK maps for each dataset was evaluated by running five times in both approaches; means and standard deviations were calculated. NRMSE value was calculated by using equation $NRMSE = \sqrt{\Sigma(A-B)2/Length(A)}\,) . / \sqrt{(Max(B) - Min(B))}$ (3) for different matrix dimensions of 64x64, 128x128, 256x256, 512x512 with 32 time points, where A is GT, B is the EV from curve fitting of both approaches.

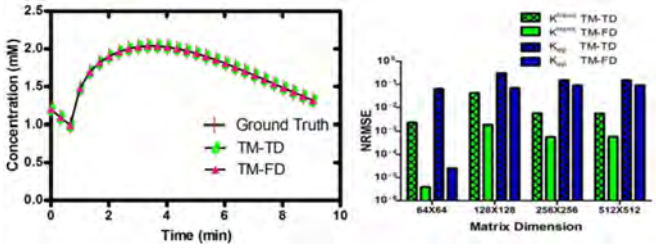

Figure 1: Comparison between TD and FD approaches, (a) CTCs fitted to model, (b) NRMSE values for K^{trans} and K_{ep}.

Matrix Dimension	Time Taken (min)		Time Difference (min)	Percentage Difference (%)
	TM-TD	TM-FD		
32x32	0.98±0.02	0.76±0.009	0.22	21.66
64x64	3.85±0.04	3.22±0.11	0.63	16.32
128x128	16.16±0.64	12.11±0.15	4.05	25.04
256x256	60.66±0.23	47.66±0.93	13	21.34
512x512	240±2.41	185.83±3.31	54.17	22.56

Table 1: Time comparison between TM-TD and TM-FD

Results and Discussion: *Simulation results:* Figure 1a depicts example of CTCs fitting obtained using equations 1 and 2 in simulated data. The demonstrated TM-FD resulted in similar fitting in comparison to both TM-TD and GT taken. NRMSE graphs for K^{trans} and Ve maps of both approaches, using the output of curve fitting on the original data as GT was measured and plotted in log scale in Figure 1b. The demonstrated TM in FD approach produces lower NRMSE values over the range of different matrix dimension. Table 1 depicts the time taken for curve fitting in min from both approaches indicating strict bounds on the means. It can be observed that there is significantly lesser standard deviation in both approaches demonstrating the Goodness Of Fit (GOF). The simulated data results show a good fit of the demonstrated model with less computational time. *In-vivo data results:* Figure 2a depicts tumor ROI drawn for breast DCE datasets, 1st column of Figure 2b and Figure 2c depicts the K^{trans} and Ve maps of the tumor of dataset 1 respectively (shown as magnified version in red outline) using TM in TD and TM-FD and so on. TM in FD was able to reproduce similar PK maps as that to TM in TD with lesser computational time taken. **Conclusion:** Accelerated determination of PK maps using TM in FD was achieved and could reliably substitute for TM in TD with significantly lesser computational time. Current and future work involves applying of this approach to other existing models like Extended Tofts Model (ETM) and subsequent radiological evaluation (blind). **References:** [1] Steven P. Sourbron et al, MRM 2011 [2] Nithin N Vajuvalli et al, IEEE EMBS, 2014 [3] Wei Huang et al, Translational Oncology 2014 [4] michallenges.org/dceChallenge2/clinical.html. **Acknowledgement:** Dattesh D shanbhag, GE ITC, Bangalore for helpful discussions.

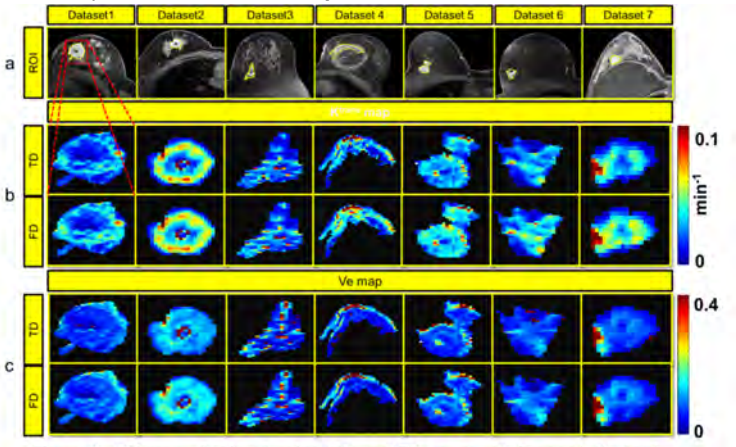

Figure 2: PK map obtained using TD and FD approach for each dataset