Optimal Sampling Design in Quantitative DCE MRI

Ina Nora Kompan[1,2] and Matthias Guenther[1,2]
[1]*Fraunhofer MEVIS, Bremen, Bremen, Germany,* [2]*mediri GmbH, Heidelberg, Baden-Württemberg, Germany*

Introduction: In dynamic contrast-enhanced (DCE) MRI, pharmacokinetic (PK) modeling is used to quantify tissue physiology. The Tofts model[1] quantifies the parameters K^{trans}, v_e and the onset time τ. For fitting accuracy, high temporal resolution is needed whilst high spatial resolution is required to depict heterogeneities of PK maps. A trade-off is to sample at high temporal/low spatial resolutions at times which are sensitive to fitting and otherwise at low temporal/high spatial resolutions. In this work, optimal sampling design is applied to the Tofts model to determine sampling times which have the highest impact on fitting accuracy. From the resulting optimal sampling schemes (OSS) it is derived where fast sampling is necessary and where slow sampling is sufficient. The performance of OSS and equidistant sampling schemes (EDS) is compared. This method was previously applied to arterial spin labeling data[2].
Here, the applied methods are adjusted for DCE MRI.

Methods: The Tofts model[1] with a population-averaged arterial input function[3] is used as underlying model. Based on the Fisher information approach[2], the OSS for a varying number of time points N=6,...,40 at sampling times t_i are derived for the parameter set $\mathbf{p}$=(K^{trans}=2.0min^{-1},v_e=0.8, τ=1.5min). Between adjacent time points, a minimal interval Δt_{min}=10s allowing for image acquisition is assumed. To compare the performance of the OSS and the EDS, a Tofts model curve with parameters $\mathbf{p}$ is generated and Gaussian noise of two standard deviations σ_1/σ_2=0.01/0.05 is added. The noisy curve is resampled to the time points of the EDS and OSS and the Tofts model is fitted to the new curves. This process is repeated 100 times, providing resulting parameters $\{\mathbf{p}_{fit}\}$. The relative mean values K_{fit}, v_{fit} and τ_{fit} and standard deviations (SD) $\sigma_{K,fit}$, $\sigma_{v,fit}$ and $\sigma_{\tau,fit}$ are calculated. Additionally, the OSS of a distribution of parameters $\mathbf{p}_\delta$=(0.2min^{-1}<K^{trans}<2.5min^{-1}, 0.2<v_e<1.0, 1.5min<τ<1.6min, increments of 0.01), is determined. The OSS for each parameter set within $\mathbf{p}_\delta$ is calculated separately and the resulting OSS are collected in a histogram. Division of the area under the histogram by N yields the OSS of the distribution. In this work, the OSS for N=10 sampling points is calculated.

Results: In figure 1, the time points of OSS for varying N are plotted. For small N, sampling times are clustered in the interval [τ,τ+2min]. With increasing N, samples times are added to the next possible higher times within the constraints of Δt_{min}. Finally, sample points are placed at the baseline. The comparison of the EDS and OSS is shown in figure 2. For small N, the EDS exhibits large mean errors, following a zig-zag pattern with large SD, whilst for the OSS they are significantly smaller. With increasing N, the EDS approaches the performance of the OSS. For large N, both the OSS and EDS approach a constant noise-dependent standard deviation. K^{trans} is the most unstable parameter, whilst v_e is more stable. τ is stable for the OSS, whilst for the EDS it is only stable for large N. The resulting OSS of the distribution is displayed in figure 3. High temporal sampling is required for the first 2min after τ.

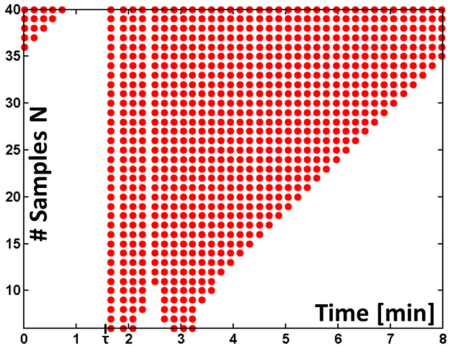

Figure 1: OSS for varying numbers of sampling times N. The red dots indicate sampling times.

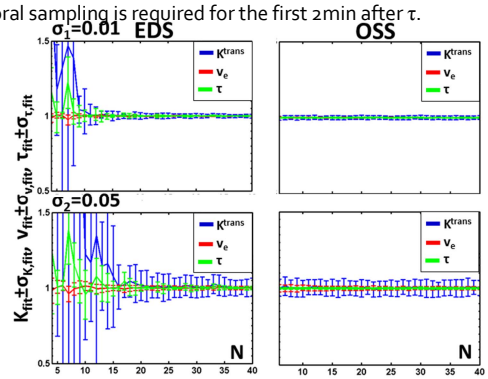

Figure 2: Comparison of the performance of the OSS and EDS for two noise standard deviations σ_1 and σ_2

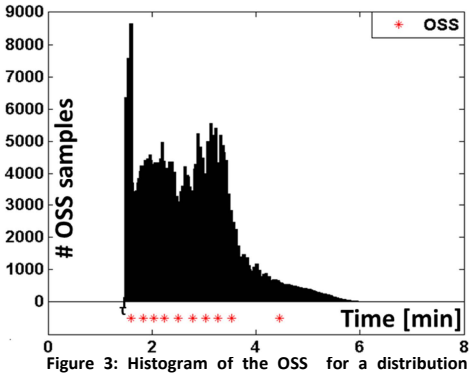

Figure 3: Histogram of the OSS for a distribution of parameter sets and the resulting OSS of the distribution.

Summary & Discussion: In this work it is derived, using optimal sampling theory, where fast sampling is needed for Tofts model fitting and where slow sampling can be exploited for high spatial resolution. It is found that fast sampling during the first 2min after τ is needed for high fitting accuracy. It is shown that optimal sampling outperforms equidistant schemes for small N. The large errors of the EDS for small N arise from missing important samples at the onset and the initial upslope, which are K^{trans} - and τ-sensitive, leading to large overestimation of τ and K^{trans}. For the OSS, the sensitive interval
[τ, τ +2min] is sampled for all N, providing more stable fitting. Accurate K^{trans} fitting is especially important due to its high clinical importance[4]. Furthermore, for all N, fitting accuracy is strongly governed by noise, which should be taken into account. It should be kept in mind that the results are only valid for the assumed model and underlying parameters, which could be unsuitable to describe reality. However, this method can be straightforwardly applied to other models and underlying parameters. Still, the resulting OSS is in good agreement with clinical studies[5-7], where combined resolution schemes were shown to improve diagnostic performance. For *in vivo* applications, τ is not known prior to imaging. Therefore, bolus tracking would be of advantage. It should also be
taken into account that faster sampling may degrade image quality, imposing further fitting errors.

References: 1) Tofts PS, et al.Magn Reson Med.1991;17:357-267.2) Xie J, et al.Magn Reson Med.2008;59:826:834.3) Walker-Samuel S. PhD Thesis. University of London, 2007.4) Leach, et al. British Journal of Cancer 2005;92:1599-1610.5) Pinker K, et al.Invest Radiol.2009;44:553-558.6) Jansen, et al. Phys Med Biol.2010;55:473-485.7)Mann RM, et al. Proc Int. Soc Magn Reson Med. 2011