Optimal Sampling Schedule for PARACEST Agents and Analysis of its Performance

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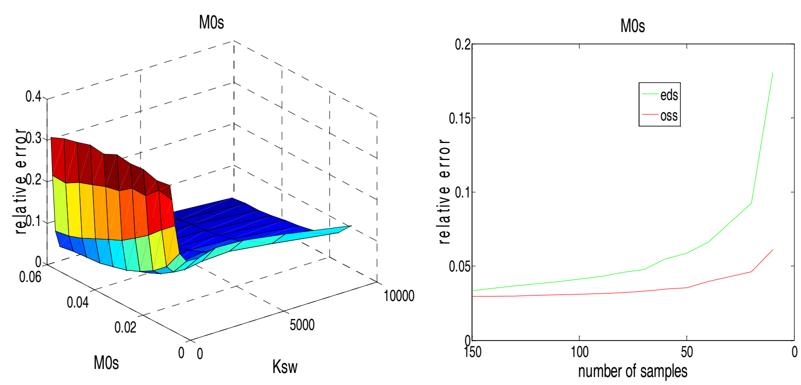
Introduction: Generally, sampling schedule for CEST imaging is to acquire the whole investigated frequency offsets with even distribution, which is called evenly distributed sampling schedule (EDS). This sampling schedule has been proved to be inefficient because some data collected are minimally informative. An optimal sampling schedule (OSS) had been proposed by Y. K. Tee et al. for DIACEST agents[1]. For the PARACEST agents, the chemical shifts of exchange protons are far away from water resonance, which makes the use of OSS very appealing. In this study simulations were conducted to validate the performance of OSS on PARACEST agents.

Methods: A two-pool chemical exchange model was set up considering: a free water pool (pool w) and a PARACEST agent pool (pool s). The PARACEST agent used in this simulation was based on Ref.[2], where the chemical shift is 56 ppm. The chemical exchange rate from pool s to pool w was denoted by $\mathbf{K_{sw}}$, and the initial magnetization of pool w and pool s in z-direction were given by $\mathbf{M_{0w}}$ and $\mathbf{M_{0s}}$. The prior information of $\mathbf{K_{sw}}$ and $\mathbf{M_{0s}}$ was described by Gaussian distributions cut off by upper bounds and lower bounds as shown in Table 1. Other parameters were treated as constant and used representative values in Ref.[2]. 100,000 random values of $\mathbf{K_{sw}}$ and $\mathbf{M_{0s}}$ were generated according to their prior distribution. Sensitivity functions[1] were calculated for each pair of random model parameters $\mathbf{K_{sw}}$ and $\mathbf{M_{0s}}$, and then were averaged to get average sensitivity curves. Instead of averaging OSS for all possible model parameters, a simpler algorithm was applied, i.e. the ultimate OSS was directly calculated by finding the maximum value of Hessian matrix[1] associated with average sensitivity curves. Simulations were performed on the distribution of parameter values to evaluate the performance of OSS. ln($\mathbf{K_{sw}}$) was varied from 5.2 to 9.2 with 10 values, $\mathbf{M_{0s}}$ was varied from 0.01 to 0.06 with 10 values. For each pair of model parameter, 1000 noisy z-spectra were produced by adding white Gaussian noise with standard deviation equaled to 0.01 of $\mathbf{M_{0w}}$. In all, 100,000 noisy z-spectra sampled by EDS and OSS (81 samples) were fed into least square curve fitting function built in MATLAB R2012a to estimate $\mathbf{K_{sw}}$ and $\mathbf{M_{0s}}$. The performance of OSS and EDS were evaluated by relative errors between the estimation results and the true values of parameters. In order to examine the performance of both sampling schedules with respect to the number of samples, OSS were calculated by varying the number of samples from 150 to 10 with a step of 5. $\mathbf{K_{sw}}$ was set to be 1400 and $\mathbf{M_{0s}}$ was set to be 0.05.

Table 1 Prior distribution of model parameters

parameter	Lower bound	Upper bound	mean	Standard deviation
M_{0s}	0	0.06	0.03	0.01
$\ln K_{sw}$	5.2	9.2	7.2	1.0

Results&Discussion: The obtained OSS with 81 samples for PARACEST is shown in Table 2. OSS acquires more samples around the offset (56ppm) of the PARACEST agent. Fig 1a shows the relative errors of $\mathbf{M_{0s}}$ acquired using OSS scheme for different exchange rates ($\mathbf{K_{sw}}$) and concentrations ($\mathbf{M_{0s}}$). It can be seen that the relative errors by OSS method is strongly affected by $\mathbf{K_{sw}}$. Generally, higher precision is achieved for the exchange rate of 700 to 10^4 and concentration of 0.03 to 0.05. Simulation illustrated that OSS had better performance almost on the whole distribution of $\mathbf{K_{sw}}$ and $\mathbf{M_{0s}}$ compared to EDS. Fig 1b shows the performance of both sampling schedules while the number of samples decreased from 150 to 10. Results show that the relative errors is relatively small (when the number of samples is in the range: 150 to 80). As the number of samples continues to decrease, the relative error increased much more rapidly, particularly when sample number is lower than 50. The relative errors acquired by OSS are still far less than EDS method in the low sample number range.



(a) (b)

Fig 1 Relative error of estimate $\mathbf{M_{0s}}$: (a) on the possible distribution of parameters (b) while the number of samples reduced

Table 2 Optimal sampling schedule for PARACEST agent

Lower bounds	Upper bounds	Number of samples
-50ppm	-10ppm	0
-10ppm	0ppm	13
0ppm	10ppm	22
10ppm	50ppm	0
50ppm	60ppm	36
60ppm	70ppm	10
70ppm	100ppm	0

Conclusion: In this study, an optimal sampling schedule was proposed and verified for better two-pool PARACEST quantification. A connection was found between the performance of OSS and the distribution of true values of model parameters. The new method is able to provide more accurate parameters comparing to EDS scheme in the same experimental time. Simulation shows that the number of samples should be kept above 50 to assure adequate precision.

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Refernces:[1]Y. K. Tee, A. A. Khrapitchev et al, MRM, 70:1251-1262, 2013; [2]Donald E. Woessner, Shanrong Zhang et al, MRM, 53:790-799, 2005.