Comparison of Linear and Non-linear Fitting Methods for Estimating T1 from SPGR Signals

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Introduction: T1 maps can be computed from spoiled gradient recalled echo (SPGR) images acquired with different repetition times (TRs) and/or flip angles. Recently, the acquisition of high resolution T1 maps in a clinically feasible timeframe has been demonstrated with Driven Equilibrium Single Pulse Observation of T1 (DESPOT1) [1]. DESPOT1 derives T1 from two or more SPGR images acquired with constant TR and different flip angles using linear least-squares (LS) fitting of a linear transformation of the function relating signal intensity, flip angle, TR, T1, and equilibrium longitudinal magnetization [1, 2]. Linear fitting has the advantage of being computationally fast, however, non-linear fitting approaches could be preferable if they provide better accuracy and precision of the estimated T1. Few papers have investigated the impact of fitting procedures on the precision of T1 estimated from SPGR signals [1-3], but the impact on T1 accuracy is essentially unexplored. Here, we provide a systematic evaluation of accuracy and precision of T1 calculated with both linear and non-linear fitting methods using Monte Carlo simulations of sets of SPGR signals produced assuming various experimental conditions.

Method: The measured SPGR signal intensity can be written as $S_j = \frac{M_0(1 - E_i)\sin(\alpha)}{1 - E_i \cos(\alpha)} + N_i$ (1), where $\alpha$ is the flip angle, $M_0$ is the equilibrium longitudinal magnetization, $N_i$ is the random noise function, and $E_i = \exp(-\frac{TR}{T1})$ [1, 2]. The non-linear LS approach estimates $T1$ and $M_0$ from equation (1) by minimizing the equation: $f_{NL}(M_0, T1) = \sum_{i=1}^{N}(S_i - \hat{S}_i)^2$. We tested two non-linear fitting methods, Levenberg-Marquardt (LM) [4] and Modified Full Newton (MFN) [5]. Linear fitting can be used if all images in the dataset are collected with the same $TR$ and the noise term is neglected. Under these conditions equation (1) can be represented in linear form as: $\frac{S_j}{\sin(\alpha)} = E_i \frac{S_j}{\tan(\alpha)} + \frac{M_0(1 - E_i)}{\cos(\alpha)}$ (2). We used a linear LS method to compute $T1$ and $M_0$ from equation (2) similarly to what was previously proposed [1, 2].

Simulations: We performed simulations of different experimental designs, (TRs, flip angles) and different expected values of $T1$. Different signal to noise (SNR) levels were simulated by adding (in quadrature) Gaussian noise with zero mean and variable standard deviation ($\sigma$) to the noise-free SPGR signals generated using equation (1). Results reported below are computed assuming TR=10ms, $T1$=1000ms and $M_0$=3000, optimal flip angles [2] of 19.3 and 3.4 degrees, 2, 4, 6, 8, 16, or 32 SPGR images with repeated optimal angles, and SNR (expressed as $M_0/\sigma$) ranging from 100 to 600.

Results: Figure 1 shows the distributions of $T1$ obtained with linear and nonlinear methods at two different SNR levels. The variability of $T1$ is similar in both linear and nonlinear cases but the distribution of $T1$ is biased (shifted to the left) in the linear case. This bias is more pronounced at low SNR. Figures 2 and 3 show the mean and the standard deviation (SD) of $T1$ as a function of the number of data points. As the number of data points increases, the SD decreases for both the linear and non-linear cases. Surprisingly the mean value appears progressively more biased as the number of data points increases when linear fitting is used (Fig. 2). At very low SNR, the estimated $T1$ using LM non-linear fitting was found to be unstable with a high occurrence of negative $T1$ values; the MFN approach was less susceptible to this problem (data not shown).

Discussion: The main goal of this study was to establish if fitting SPGR data to a non-linear model would provide better estimates of $T1$ than the conventional approach of fitting data to a linear model. Regarding $T1$ variance, linear and non-linear approaches appear equivalent over a wide range of experimental conditions. However, $T1$ estimates using linear fitting are biased. The accuracy of $T1$ is improved as the number of data points is increased with non-linear fitting, but paradoxically is decreased with linear fitting. Overall, non-linear fitting would appear to be the preferred method for computing $T1$ from SPGR data, however, the instability of non-linear fitting at low SNR is disconcerting. We suspect that this instability is due to the known large residuals problem [4], but more work is needed to fully elucidate $T1$ estimation in the low SNR regime.