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

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Introduction: T_1 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 T_1 maps in a clinically feasible timeframe has been demonstrated with Driven Equilibrium Single Pulse Observation of T_1 (DESPOT1) [1]. DESPOT1 derives T_1 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*, T_1 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 T_1. Few papers have investigated the impact of fitting procedures on the precision of T_1 estimated from SPGR signals [1-3], but the impact on T_1 accuracy is essentially unexplored. Here, we provide a systematic evaluation of accuracy and precision of T_1 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 $S_i = \dfrac{M_0(1-E_1)\sin(\alpha)}{1-E_1\cos(\alpha)} + N_i$ (1), where α is the flip angle, M_0 is the equilibrium longitudinal magnetization, N_i is the random noise function, and $E_1 = \exp(-\frac{TR}{T_1})$ [1, 2]. The non-linear LS approach estimates T_1 and M_0 from equation (1) by minimizing the equation: $f_{NLS}(\hat{M}_0, \hat{T}_1) = \sum_{i=1}^{n}\left(S_i - \hat{S}_i\right)^2$. 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: $\dfrac{S_i}{\sin(\alpha)} = E_1\dfrac{S_i}{\tan(\alpha)} + M_0(1-E_1)$ (2). We used a linear LS method to compute T_1 and M_0 from equation (2) similarly to what was previously proposed [1, 2].

Simulations: We performed simulations of different experimental designs, (*TR*s, flip angles) and different expected values of T_1. Different signal to noise (SNR) levels were simulated by adding (in quadrature) Gaussian noise with zero mean and variable standard deviation (σ) to the noise-free SPGR signals generated using equation (1). Results reported below are computed assuming *TR*=10ms, T_1=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/σ) ranging from 100 to 600.

Results: Figure 1 shows the distributions of T_1 obtained with linear and nonlinear methods at two different SNR levels. The variability of T_1 is similar in both linear and nonlinear cases but the distribution of T_1 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 T_1 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 T_1 using LM non-linear fitting was found to be unstable with a high occurrence of negative T_1 values; the MFN approach was less susceptible to this problem (data not shown).

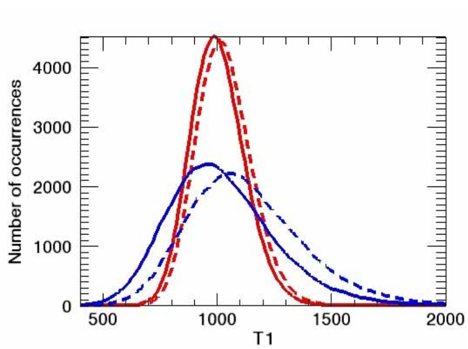

Fig. 1 The distribution of T1 using 6 points (3 replicates of optimal angels) with 2 different noise levels. (red: M_0/σ=200, blue: M_0/σ=100, solid line: non-linear, dashed line: linear) The true T1 value is 1000 ms.

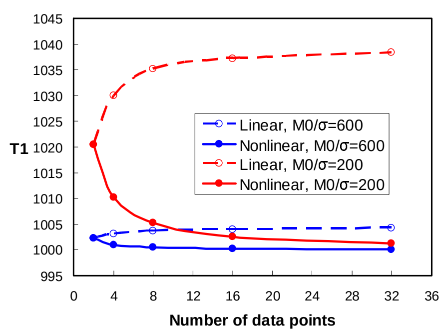

Fig. 2 Mean estimated T1 value using linear and non-linear methods with increasing number of data points and at different noise levels (red: M_0/σ=200 and blue: M_0/σ=600). The true T1 value is 1000 ms.

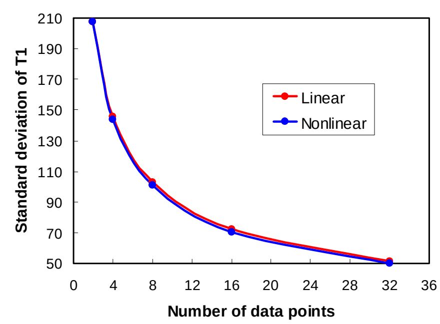

Fig. 3 The standard deviation of T_1 using linear and non-linear fitting with increasing number of data points (*TR*=10ms, T_1=1000ms M_0/σ =200).

Discussion: The main goal of this study was to establish if fitting SPGR data to a non-linear model would provide better estimates of T_1 than the conventional approach of fitting data to a linear model. Regarding T_1 variance, linear and non-linear approaches appear equivalent over a wide range of experimental conditions. However, T_1 estimates using linear fitting are biased. The accuracy of T_1 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 T_1 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 T_1 estimation in the low SNR regime.

Reference: [1] Deoni et al, *Magn Reson Med* 49: 515-526, 2003. [2] Wang et al, *Magn Reson Med* 5: 399-416, 1987. [3] Deoni et al, *Magn Reson Med* 51: 194-199, 2004. [4] Nocedal et al, *Numerical Optimization*, Springer, 1999. [5] Koay et al, *J. Magn Reson.* 182:115-125, 2006