# Derivation of optimal flip angles via minimization of noise factor over large range of T1 for accurate variable flip angle-derived T1 estimations

**K. Miyazaki[1], D. J. Collins[1], D-M. Koh[1], D. J. Hawkes[2], M. O. Leach[1], and M. R. Orton[1]**

[1]Cancer Research UK Clinical Magnetic Resonance Research Group, Institute of Cancer Research, Sutton, Surrey, United Kingdom, [2]Centre for Medical Image Computing, Department of Medical Physics, University College London, London, United Kingdom

**Introduction:** Accurate estimation of longitudinal relaxation times (T1) is essential in many areas of MRI, such as dynamic contrast enhanced MRI and tissue segmentation. The variable flip angle (VFA) method, which utilizes spoiled gradient echo (GE) images acquired using different flip angles (θ), allows relatively accurate estimation of T1 in a short time period compared to lengthy inversion recovery methods [1]. In order to further reduce total scan time, it would be advantageous to use just two spoiled GE data acquired using two different flip angles. By minimizing the noise factor (NF), Wang HZ *et al* have shown that for every T1 at a given repetition time (TR) there exists an optimal (or tuned) set of two flip angles which allow accurate estimation of T1 [2]. However, optimization of flip angles when imaging samples consisting of large T1 ranges has been far from trivial. Past techniques have involved manipulation of the flip angles tuned to the lower and higher T1s of the T1 range to derive their 'optimal' combination of flip angles [2, 3]. Here, we propose a simple and efficient method of obtaining this optimal set of flip angles by minimizing the area of the noise factor curve over the T1 range of interest.

**Theory:** In the VFA method, T1 is calculated from the gradient of the linear plot of $S_i/\sin\theta_i$ against $S_i/\tan\theta_i$ where $S_i$ is the signal of a spoiled GE sequence acquired using $\theta_i$. An expression for the variance in T1 due to uncertainty in the signal ($\sigma^2_{T1}$) can be obtained from the standard formula for noise propagation. The noise factor (NF) as defined by Kurland RJ [4] is then given by the following expression:

$$\mathrm{NF} = \left[\frac{\sigma_{T_1}/T_1}{\sigma/M_0}\right] = \frac{T_1 e^{TR/T_1}}{TRN(\bar{X}^2-(\bar{X})^2)}\left[\sum_{i=1}^{N}\left[\frac{X_i-\bar{X}}{\sin\theta_i}+\frac{Y_i-\bar{Y}-2e^{-TR/T_1}(X_i-\bar{X})}{\tan\theta_i}\right]^2\right]^{1/2}$$

where $M_0$, σ and N are spin density, noise and the number of flip angles respectively. $X_i = s_i/\tan\theta_i$ and $Y_i = s_i/\sin\theta_i$ respectively where $s_i = \frac{(1-e^{-TR/T_1})\sin\theta_i}{1-e^{-TR/T_1}\cos\theta_i} = \frac{S_i}{M_0}$

Our optimization method involves the analysis of NF over a range of T1 values of interest using different combinations of flip angles. The area under the curve of NF vs. T1 is evaluated for all flip angle combinations and the pair of flip angles which corresponds to the minimum area is defined as our optimal set of flip angles. These flip angles will be referred to as $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$.

**Materials & Methods:** $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$ were calculated as described above by simulating $s_i$ with a fixed TR of 4.36 ms (since this is used in our clinical protocol.), T1 ranging from 50 to 1300 ms (range observed in DCE-MRI studies) and different flip angles. Using $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$, NFs for the different T1 values in the range were then calculated. Our results were compared to the ideal case where NFs for individual T1s are calculated using optimal sets of flip angles tuned to the respective T1s. These individually tuned flip angles are shown in figure 1. A comparison was also made to the approach taken by Wang when estimating T1 in a sample with a large range of T1 [2]. Both phantom (Eurospin II phantom consisting of 12 tubes filled with agarose gel and doped with varying amounts of gadolinium) and volunteer scans were performed on a Siemens Avanto, 1.5T system with a phased array body coil. 3D spoiled GE images were acquired using the following sequence parameters which were fixed in every scans: TR/TE/NSA/partition thickness/number of partitions/FOV/matrix size/GRAPPA = 4.36 ms/1.32 ms/1/5 mm/20/350 x 350 mm$^2$/256 x 256/2. θ was varied at $\theta_{1,\,AUC}$, $\theta_{2,\,AUC}$, $\theta_{1,\,WANG}$ and $\theta_{2,\,WANG}$. 2 sets of T1 maps were generated using the VFA method by combining data acquired using flip angles optimized using our approach and Wang's approach respectively. Regions-of interest (ROIs) were drawn around the different gels on phantom T1 maps, and around the fat, liver and intercostal muscles on in-vivo T1 maps. Means and standard deviations (sd) of T1 values derived from the ROIs were compared between the two approaches. Further simulations were carried out as above for TR values of 3, 4, 5 and 6 ms to determine respective values of $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$. These TR values are typical of those used in DCE-MRI studies.

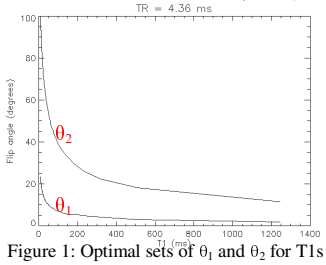


Figure 1: Optimal sets of $\theta_1$ and $\theta_2$ for T1s ranging from 0 to 1300 ms and TR = 4.36 ms as defined by Wang HZ in reference 1.

**Results:** The global minimum of the simulation was found at flip angles of $\theta_{1,\,AUC} = 3°$ and $\theta_{2,\,AUC} = 16°$. The variation of NF calculated using these optimal flip angles is shown in figure 2 (red line) together with the ideal case (black dashed line). $\theta_{1,\,WANG}$ and $\theta_{2,\,WANG}$ were 6° and 32° for the T1 range and TR used in the simulation. NF calculated using these flip angles varies with T1 is shown by the blue curve in figure 3. T1 values of the Eurospin II phantom gels calculated using $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$ were found to agree better with both the manufacturer provided T1 values and values calculated using an inversion recovery turbo-FLASH technique [5] than T1 values calculated using $\theta_{1,\,WANG}$ and $\theta_{2,\,WANG}$. In-vivo T1 values obtained from the organ ROIs are tabulated in table 1. T1 values obtained using our approached agreed well with the literature values [6]. $\theta_{1,\,AUC}$ and $\theta_{2,\,AUC}$ for different TR values are shown in table 1.

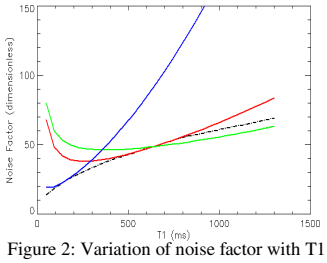


Figure 2: Variation of noise factor with T1 in the ideal case (black dashed), our proposed approach (red) and Wang HZ's approach (blue). NF is reduced significantly in our approach compared to Wang HZ's approach (n.b. blue curve goes off the scale at higher T1).

**Discussions:** Using our approach to derive the optimal flip angles, NF in the mid-T1 range is comparable to that of the ideal case as seen from the overlap of the red and black-dashed curves between 400 and 900 ms in figure 3. This indicates that over this range of T1, the standard deviation in T1 due to uncertainty in the signal ($\sigma_{T1}$) is minimal. Compared to Wang's approach (blue curve), our approach results in significantly reduced NF over a large range of T1, most markedly at high T1s (> 500 ms). At lower T1s (< 500 ms), NFs using our approach is only slightly inferior. (Note that the blue curve goes off the scale at larger T1s, indicating Wang's approach is not optimal for the T1 range and TR of interest in this study). Simulation results are supported by results from both phantom and in-vivo studies. Data in table 1 were generated to aid the readers to appreciate the set of flip angles optimized using our technique for their rough TR of interest. Although not described above due to lack of space, our method was compared to a previously reported three flip angles optimization approach [3]. NF calculated using the three flip angles (2°, 11°, 18°) optimized using their method varies with T1 as shown by the green curve in figure 3. It can be seen that our two flip angles optimization approach is comparable to the previously reported three flip angles optimization approach.

| Organ | Mean (sd) T1 (ms) | | |
|---|---|---|---|
| | Our approach | Wang's approach | Literature |
| Liver | 585 (175) | 834 (129) | 586 (39) |
| Fat - right | 327 (23) | 373 (126) | 342 (37) |
| Fat – left | 311 (51) | 324 (107) | 342 (37) |
| Intercostal muscle | 1099 (178) | 1577 (928) | 856 (61) *paravertebral muscle |

Table 1: Statistically summarized T1 values of different organs calculated using our approach and Wang's approach. Mean T1 values of our approach agreed well with literature values [6, 7] whilst those calculated using Wang's approach were higher, especially in organs with higher T1s (i.e. the liver and the intercostal muscle)

| | TR (ms) | | | |
|---|---|---|---|---|
| | 3 | 4 | 5 | 6 |
| $\theta_{1,\,AUC}$ | 2 | 3 | 3 | 3 |
| $\theta_{2,\,AUC}$ | 14 | 16 | 18 | 20 |

Table 2: Optimized flip angles calculated using our approach for different TRs ranging from 3 to 6 ms.

**Conclusions:** This work has shown that pairs of optimal flip angles for calculation of T1 using the variable flip angle method can be derived by minimizing the area under the noise factor curve over the T1 range of interest. Using these optimized flip angles, estimations of T1 with reduced error in T1 can be carried out over a large range of T1 using just two spoiled gradient echo acquisitions and the result is comparable to using three acquisitions. This optimization approach is simple and effective and it is an objective method which takes into account the whole range of T1 values which has not been the case in previously reported optimization works. Our proposed method would enable accurate quantification of T1 over a large range which is beneficial in numerous areas in MRI. It is of particular importance in DCE-MRI studies where accurate determination of T1 is crucial in obtaining quantitative parameters which are widely used to monitor disease progression and regression.

**References:** [1] Fram EK. MRI 1987; 5(3):201-208 [2] Wang HZ, et al. Magn Reson Med 1987; 5:399-416 [3] Cheng H-LM, et al. Magn Reson Med 2006; 55:566-574 [4] Kurland RJ. Magn Reson Med 1985; 2:136-158, [5] Hasse A. Magn Reson Med 1990; 13:77-89 [6] de Bazelaire CM. Radiology 2004; 230(3):652-659

**Acknowledgements:** This work was supported by Cancer Research UK (C1060/A5117) and EPSRC (GR/T20427/01)