Determining precision of relaxation time measurements: application to T2 mapping

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Introduction: Relaxation time constants allow quantitative analysis of tissues and in vivo measurement of contrast agent concentrations. Accuracy and precision of the mappings are affected by a number of effects, including system imperfections (B_0 and B_1 inhomogeneity, eddy-currents …) and noise. Usually, reproducibility is assessed, by comparing relaxation time values across regions of interests (ROI) in multiple patients [1]. Reproducibility in this sense also includes the effect of e.g. patient preparation and positioning, but also size and placement of the ROI. Generally, little is known on the precision of the individual experiment performed in a specific subject. Here, a method is presented that calculates a map of the relaxation time standard deviation (SD), from a single mapping experiment, accounting for the noise level of the input images and the sequence parameters. The proposed method was evaluated in simulations and in vivo in T_2 mapping of the knee.

Theory: Maximum likelihood (ML) methods allow for accurate and precise estimation of relaxation times [2]. Provided a correct modelling of the underlying process and of the noise statistics, ML estimators are asymptotically unbiased and reach the minimal variance level (Cramer-Rao lower bound) [3]. For most MR acquisitions, including Fourier and sensitivity encoding, noise of complex images follow a Gaussian distribution. Since ML estimation with Gaussian statistics can be done by means of fast least-squares optimization algorithms, it is more convenient to use the complex images for computation, although ML estimation from magnitude images is also possible [4]. The complex signal s of a multi-echo spin-echo sequence with echo times TE_k, $1 \le k \le N$, can be described with the following model:

$$s_k(\beta) = \rho_0 \, e^{i\varphi_0} e^{-TE_k/T_2} . \qquad (1)$$

Here, ρ_0 and φ_0 denote the initial signal amplitude and phase, and $\beta = (\rho_0, \varphi_0, T_2)$. This model assumes perfect refocusing of the spins at the echo times TE_k, and neglects the influence of stimulated echoes. Estimation of the model parameters β from the complex data y_k is carried out by minimizing the penalty function:

$$L(\beta) = \frac{1}{\sigma^2} \sum_{k=1}^{N} \left\| y_k - s_k(\beta) \right\|^2 \qquad (2)$$

where σ is the noise SD. The covariance matrix of the estimated parameters $\hat{\beta}$ can be derived from the Jacobian Matrix of L:

$$Cov(\beta) = \left(J^T J \right)^{-1} \text{ with } J_{ij} = \partial s_i(\beta) / \partial \beta_j \qquad (3)$$

It follows from the properties of ML estimation [3] that the penalty function $L(\hat{\beta})$ has a chi-square distribution with $2N$-3 degrees of freedom, and the estimator $\hat{\beta}$ has a Gaussian distribution with covariance matrix given by Eq. (3).

Methods: Accuracy and precision of the ML estimator were first assessed using Monte-Carlo simulations, for different values of relaxation time, initial signal amplitude, and number of echoes. Constant noise SD and echo spacing were assumed. The bias $\hat{\beta}_i - \beta_i$ and the coefficient of variation (COV) $\sqrt{Var(\hat{\beta}_i)} / \beta_i$ were computed and compared with the COV value predicted by Eq. (3). Then, multi-echo spin-echo images for T_2 mapping in the knee (7 echoes, 12.5ms echo spacing, resolution 0.4×0.6×3mm, TR=3500ms) were acquired on a 3T scanner (Achieva, Philips Medical Systems) in 3 volunteers. For each volunteer, two scans were performed consecutively. Maps of T_2, of the penalty function, and of the T_2 SD were computed with the ML algorithm. A chi-square test with 11 degrees of freedom was applied to the penalty function map to identify pixels, for which the model was inaccurate. The validity of the predicted SD values was tested: the difference in the two T_2 maps, normalized pixel-wise by the root-sum-of-squares of the two predicted SD maps, was computed. The SD of this ratio, which is expected to be Gaussian with unit SD, was computed for selected ROIs.

Results: Fig. 1 shows an example of simulation results for N=7, ρ_0/σ=20, and 12.5 ms echo spacing. A small bias is present for large T_2, but this bias vanishes, when the number of echo times increases (not shown). The predicted coefficients of variation closely match those computed from the Monte-Carlo simulations. Note that the COV significantly varies over the range of T_2 values. Fig. 2 shows a T_2 map with its corresponding COV map. The chi-square test on the penalty function rejected 3% of the pixels, primarily vessels. Tab. 1 summarizes the SD values of the normalized T_2 map differences. The values obtained for selected ROIs are very close to 1.0, indicating a good agreement between the predicted T_2 SD and the observed statistical fluctuation due to noise.

Discussion and conclusion: Although the ML estimator is only asymptotically unbiased with variance given by the Cramer-Rao bound, the simulations show that this property also approximately holds with a small number of echoes. The SD maps (or equivalently the COV maps) allow assessing precision of T_2 values on a per pixel basis. This was confirmed in vivo by comparison with T_2 difference maps obtained from repeated acquisitions. Knowing the SD, the significance of (localized) relaxation time changes over experiments can be more precisely stated. In conclusion, ML estimation is well suited for the computation of relaxation times and the assessment of precision. Given an accurate model of the signal behaviour and information on the noise statistics, the method can be readily extended to other relaxation mappings.

References: [1] Glaser et al, MRM, 56:527-534 (2006). [2] Karlsen et al, MRM, 41:614-623 (2006). [3] Rao, 1973. [4] Sénégas et al, ISMRM, #1782 (2007).

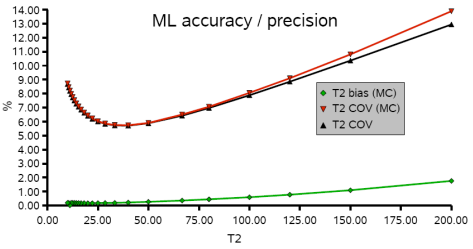

Fig. 1: Bias and COV of the ML estimator computed with Monte Carlo (MC) simulations, and compared to the predicted COV.

Cartilage				Bone	Muscle	All
Fem. med.	Fem. lat.	Tib. med.	Tib. lat.	marrow		
0.99	1.24	0.92	1.00	1.06	0.87	1.01

Table 1: SD of the normalized T_2 map differences for selected ROIs.

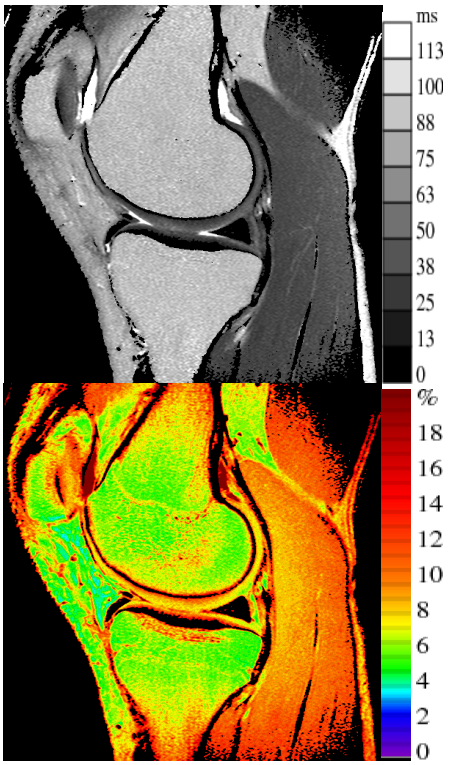

Fig. 2: Slice of a sagittal T_2 map (top) of the knee, with its corresponding COV map (bottom).