Determining uncertainty in estimates of relaxation time (T2) and proton density (S0) derived from T2 –weighted MRI using bootstrap method

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1. Introduction: T_2 is a quantitative indicator for characterizing brain tissue properties because T_2 varies significantly for grey and white matter due to their microstructure [1]. T_2 mapping has been applied in human brain tissue classification [2], animal modelling [3], and even in clinical diagnosis [4]. To increase accuracy, considerable effort has gone into minimizing various errors (scanner errors, sampling errors, and physiologically induced biases), but problems remain.

The accuracy of the estimate of (S_0, T_2) lies at the heart of S_0- and T_2-mapping. However, we often have a situation in which the estimate of (S_0, T_2) tends to be on the high side or low side of the true values. Which should we believe? To measure the uncertainties of (S_0, T_2), one way would be to obtain multiple T_2–weighted datasets from a subject and repeat the fitting procedure for the same anatomic location. But using many datasets of each subject to fit (S_0, T_2) will cost both scanning time and subject compliance. An alternative method is to use the bootstrap approach, a non–parametric statistical method. It has been used in estimating the uncertainty of the diffusion coefficient [5], [6], [7], and T_1 values [8], [9]. Here, we use the bootstrap approach to investigate distributions of (S_0, T_2) from real MR data, T_2-weighted human brain images, and examine the influence of voxel size on the reliability of (S_0, T_2) derived from fitting a mono–exponential function.

2. Methods: Images were acquired on a Siemens 3T Trio using the T_2-weighted spin echo sequence (TR/TE=1000/14ms, FoV=256mm×256mm, voxel=2×2×5mm^3). For a single slice, 32 images with varying T_2 contrast were acquired from a healthy adult. To generate bootstrapped resamples, the scan was repeated six times in a single session (without removing the subject in scanner). We have 6 T_2-weighted datasets.

From these six datasets, we generated the bootstrapped resamples by randomly selecting measurements with replacement (Fig.1). If we pooled data from the 6 datasets by randomly drawing samples, we could have $(6)^{32}\approx 7.9\times10^{24}$ datasets. In our calculations we used n=60,000 resamples to infer the distributions or the uncertainties of (S_0, T_2) for a single voxel. First, we used each dataset to fit the mono-exponential, $S(t_k) = S_0\exp(-t_k/T_2)$ $with$ $(k = 1, 2, ..., 32)$. Then, we analysed the influence of the voxel size on the distribution of (S_0, T_2) for a single voxel.

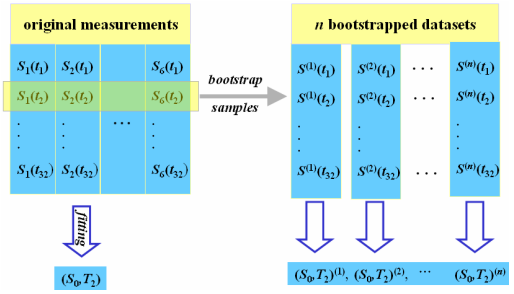

Fig.1 Illustration of the bootstrap procedures applied to measure the uncertainty of (S_0, T_2). The size of bootstrapped samples is n = 60,000 in this study.

3. Results: Fig.2 shows the distributions of (S_0, T_2) for a single voxel. The location and size of the voxel are selected in the basal ganglia, as indicated in Fig.2a. Given a voxel but with different size, our result revealed that the distributions of (S_0, T_2) are not very sharp, and their variances vary with the voxel size. Large voxel size or low spatial resolution corresponds to a small variance of (S_0, T_2). That is high spatial resolution relates to a large uncertainty.

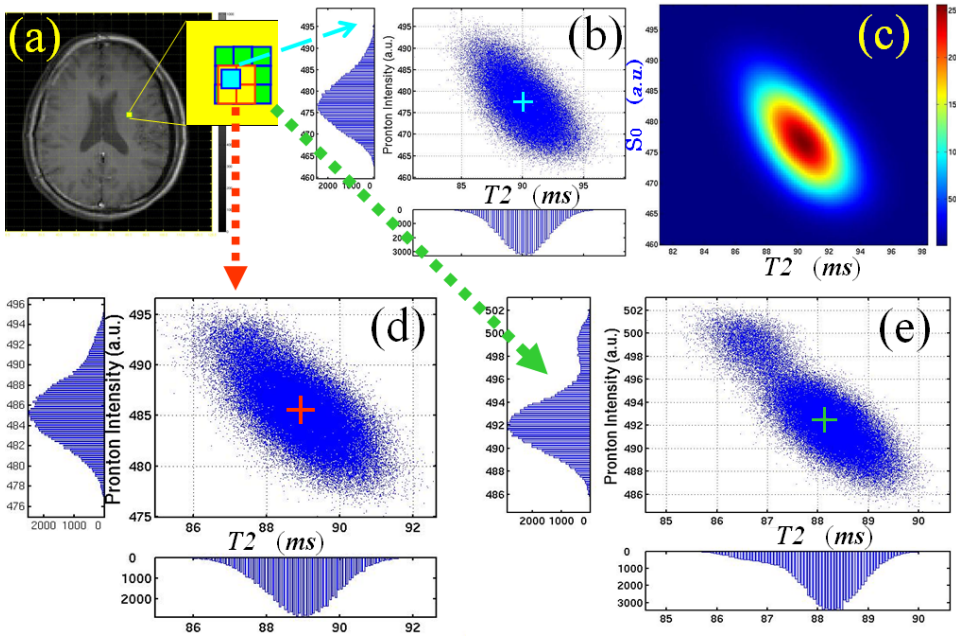

Fig.2 Influence of voxel size on the variance of S_0 and T_2 for a voxel located in the subcortical region (basal ganglia). Result indicated that variances of S_0 and T_2 are different from each other; and variances for both S_0 and T_2 increase with reducing of the voxel size. (***a***) the location of the voxel; (***b***) scatter plot of distributions of (S_0, T_2) for a voxel 2×2×5mm^3; (***c***) same to (b) but with the contour plot, the colour bar indicating the distribution scale; (***d***) scatter plot of distributions of (S_0, T_2) for a voxel 4×4×5mm^3; (**e**) scatter plot of distributions of (S_0, T_2) for a voxel 6×6×5mm^3. The size of bootstrapped samples is n = 60,000 in this study.

4. Discussion: Generally, measuring the accuracy of (S_0, T_2) is determined by two factors, "signal" and "noise" [10]. These two factors and the mathematical model influence the accuracy of the deduced parameters (S_0, T_2). Though the measure itself is sound, the values obtained from model fitting procedures often require qualification because the MR data on which they are based are of unsure quality. How well these problems are handled determines the confidence that can be placed in the accuracy of (S_0, T_2). It is usual that computer simulation often gives the impression of precision. Considering that the simulation is based on a simple assumption of the noise having a Gaussian distribution and the true noise (scanner errors, sampling errors, and physiological induced biases) do not always follow the Gaussian distribution, it is evident that determining the uncertainty with simulations is a tough challenge.

Here, we applied the bootstrap approach to real MR data for estimating the uncertainty of (S_0, T_2). The uncertainty of (S_0, T_2), shown in Fig.2, reveals a likelihood to all possible values of (S_0, T_2). The results indicate that the care must be taken if the T_2 and S_0 maps are to be used in brain tissue segmentation and clinical diagnosis. We stress that our results were obtained from fitting a mono–exponential function for a single subject. Therefore, general information regarding the variability of (S_0, T_2) for healthy human subjects is not provided and the distribution of (S_0, T_2) in this study cannot be compared with that derived from the multi–exponential case [11]. Similarly, the present study can also be used to understand T_2* maps and $T_{2\rho}$ maps because T_2* and $T_{2\rho}$ have similar relaxation equations as T_2. Usually, the distribution of (S_0, T_2) tends to be estimated after experiments. Since uncertainty is important, we can put it in at the beginning of the sequence design to improve the sequence performances.

References: [1] Fenrich et al., NMR Biomed, 14(2001)133-9; [2] Deoni et al., HBM, 25(2005) 353-9; [3] de Graaf et al., MRM, 14(2006)386-94; [4] Suzuki et al., MRI, 24(2006)877-87; [5] Pajevic and Basser, JMR, 161(2003)1-14; [6] Jones and Pierpaoli, MRM, 53(2005)1143-9; [7] Lazar and Alexander, NeuroImage, 24(2005)524; [8] Kershaw and Buckley, MRM, 56(2006)986-99; [9] Ratiney et al., MAGMA, 20(2007)143-55; [10] Swets, Science, 240(1988)1285-93; [11] Whittall et al., MRM, 47(2002)403-8.