Uncertainty of quantitative T_1 mapping in healthy volunteers at 7.0 Tesla

Daniel Polders[1], Alexander Leemans[2], Peter Luijten[1], and Hans Hoogduin[3]
[1]Radiology, UMC Utrecht, Utrecht, Netherlands, [2]Image Sciences Institute, UMC Utrecht, Utrecht, Netherlands, [3]Rudolf Magnus Institute of Neuroscience, Department of Neurology and Neurosurgery, UMC Utrecht, Utrecht, Netherlands

Introduction: Mapping of the longitudinal relaxation time (T_1) in the human brain is of great interest for both clinical research and MRI sequence development (1). For interpretation of T_1 data, it is often necessary to know the uncertainty of this quantitative parameter; without it, it is difficult to draw any conclusions about the measured variations. We combine a slice shifted multi-slice inversion recovery EPI technique (2), with a wild bootstrapping statistical method (3), leading to a procedure to determine the T_1 and its uncertainty in one short (4m10s) measurement. It is shown that the variation in T_1 over anatomic regions is larger than the uncertainty in the measurement, indicating heterogeneity of the inspected tissue. This approach to estimate the T_1 and its uncertainty without the need for repeated measurements may prove to be useful for calculating effect sizes that need to be taken into account when comparing group differences.

Methods: Nine healthy volunteers (mean age = 52.5 yr, range 34-64 yr) were scanned on a 7 T Philips Achieva MRI system. We applied a multi slice inversion recovery echo planar imaging (MS-IR-EPI) method, based on the method published by Ordidge et al (2). This method employs an adiabatic global inversion pulse followed by sequential single shot EPI readouts. By applying slice cycling the effective inversion time is varied. The acquired volume consisted of 46 single shot EPI slices. With a slice-shift of 2 slices and 23 repetitions, all slices were sampled at 23 different time points after inversion. The residuals obtained after T_1 fitting allow for estimation of the T_1 uncertainty by use of the wild bootstrap method.

The single-shot EPI sequence FOV: 224×224×91.5 mm (RL, AP, FH), voxel size 1.0×1.0×1.5 mm^3, slice gap: 0.5 mm. Inversion was achieved by a non-selective adiabatic inversion pulse. After the global inversion, all slices in the volume are acquired successively using slice-selective 90° excitations and EPI read-outs. During the second repetition the slice ordering is shifted, so all slices are acquired at a different inversion time. The total scan duration was 4 minutes and 10 seconds.

Acquired slices were re-ordered along the time direction, so that each of the 23 volumes corresponded to a specific time after inversion. After polarity restoration of the magnitude inversion curve, quantitative T_1 (qT_1) maps were calculated by fitting each voxel to:

$$I(t) = I_0 \cdot \left(1 - 2 \cdot e^{(-t/T_1)} + e^{(-TR/T_1)}\right)$$

Here $I(t)$ is the measured signal intensity at times t, T_1 is the longitudinal relaxation time to be fitted, and TR is the repetition time employed in the sequence. T_1 and I_0 were fitted by minimizing the sum of squares of the residual values of the fit and the data using a Levenberg-Marquardt optimization.

We assessed the uncertainty of the qT_1 fits using a wild bootstrap method. This method involves repeated fitting of bootstrapped data generated from the initial fit and residuals. The assumption here is that the residuals represent equivalent samples from the same noise distribution. Variations in the sampled noise cause variations in the fit, and this reflects the precision of the method. To test the uncertainty of the qT_1 fit, bootstrapped data was generated by taking the fitted curve and adding or subtracting randomly chosen residuals. One hundred new datasets were fitted, and descriptive statistics were calculated. We report the coefficient of variation of the repeated fits in percentages.

Results: Figure 1 shows an example of a single axial slice, and the three different parameters resulting from the voxel-wise qT_1 fit; T_1, I_0 and the sum of the squares of the residuals, and the corresponding uncertainty maps for T_1 and I_0.

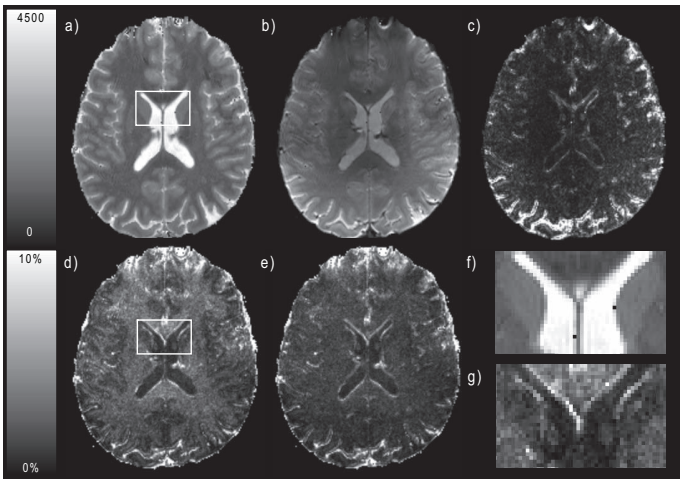

Figure 1: Overview of qT_1 parameters. a) Quantitative T_1 map of one slice. b) Fitted I_0 values. c) Residual sum of squares error. The second row displays the uncertainty in d) T_1 values and e) I_0, f) and g) show an enlargement of the boxes indicated in a) and d). Image intensities in a) and f) correspond to T_1 values as per color-bar to the left, scaling of b) and c) was set to maximize image clarity (arbitrary units). The uncertainties in d), e) and g) are scaled between 0 and 10%.

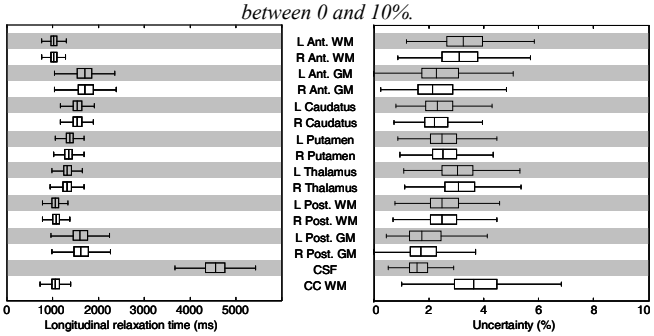

Figure 2: Group statistics for selected ROIs. Left: qT_1 values for the ROIs, considering all voxels of all subjects. Right: relative uncertainties for the same ROIs in percentages of the T_1 value. The boxes indicate the 25, median and 75 percentile of the distribution, the whiskers extend to the most extreme data points not considered outliers (outliers not shown).

For group comparison of different tissue types, several regions of interest were selected in the quantitative T_1 maps, separately for both hemispheres. Figure 2 shows the medians of T_1 values with 25 and 75 percentile ranges and the corresponding uncertainty values for the selected ROIs. These distributions are calculated for all voxels of all subjects combined, so each voxel has an equal weight. No differences in T_1 values between the left or right hemisphere could be detected. The T_1 value for cortical grey matter varies from 1779 ±356 ms (or 20.0%) to 1684 ±359 ms (21.3%). These regions also show the largest standard deviations while the uncertainties of the fits are the smallest, 1.8% to 2.3%. The T_1 values for frontal and posterior and corpus callosum white matter are 1061 ±118 ms (11.1%), 1103 ±110 ms (9.9%) and 1096 ±148 ms (13.5%) respectively, the corresponding uncertainties are 3.3%, 2.6% and 3.9%. Mean uncertainty values for the different ROIs vary between 1.9% for CSF and 3.9% for WM in the corpus callosum.

Discussion and Conclusions: The results show that this method allows for the determination of T_1 values within an uncertainty of 2-4%. The standard deviations of T_1 over the selected ROIs vary more than this; 9-20%. This indicates that tissue heterogeneity dominates the variance in the ROIs, rather than the measurement error. In general the image quality of this method is high. Although a single shot EPI readout method is applied, the distortions towards the anterior-inferior regions are relatively benign. The calculated qT_1 maps are very homogeneous, showing little or no effect of the coil transmit and receive sensitivities that are present in many other modalities at 7 T. In contrast, the fitted values for the proton density (I_0) do show these sensitivities very clearly.

The primary function of the uncertainty maps is to identify those areas where the data is not very well fitted to the model, i.e. a single T_1 component per voxel. Examples of this are found at boundaries between different types of tissue, most prominently at the ventricular wall, where partial volume effects with CSF cause the largest increase in uncertainty, see Figure 3d, e and g. This is similar to the map of residuals or sum of squares errors, which also reflects the success of the fit. However, this wild bootstrap method also allows for estimation of the uncertainty of each fitted parameter quantitatively. For example, if we consider the thalamic region, we know that it has an average T_1 of 1336 ms with an average standard deviation over this ROI of 129 ms (or 9.7%), while the mean uncertainty of the fitted T_1 values for this ROI is only 3.1%. Only part of this variation can be explained by uncertainty of the fit procedure and the SNR of the data. We are now able to say that thalamus tissue is rather heterogeneous in its T_1 value. Furthermore, when comparing groups in clinical research, differences in mean values that are smaller than the calculated uncertainty should be treated with care.

To conclude, we have shown the successful application of a multipoint multi-slice method for fast T_1 mapping with full brain coverage at high resolution. The method allows for quantitative assessment of the uncertainties of the fitted parameters, on a voxel-by voxel basis, by use of a wild bootstrap method. This approach facilitates the investigation of heterogeneity in T_1 values separately from the estimated variance of the method. By knowing the expected uncertainty in T_1 in a specific region of the brain, it is possible to interpret effect sizes in those regions. We believe that our proposed methodology contributes in making T_1 mapping a more reliable quantitative method.

References:

(1) Deoni SCL. Top Magn Reson Imag 2010;21:101-113. (2) Ordidge RJ. Magn Reson Med 1990;16:238-245. (3) Chung S. NeuroImage 2006;33:531-541.