T_2 mapping of cerebrospinal fluid: 3T versus 7T

Magnetic Resonance Materials in Physics, Biology and Medicine

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T_2 mapping with a single echo SE-EPI sequence with various TEs as truly B_1 insensitive reference for the CSF T_2 mapping sequence

Methods

SE-EPI sequence

As a reference for the CSF T_2 mapping method a single echo SE-EPI sequence was used, equal to the readout used in the CSF T_2 mapping sequence, but with increasing (very) long TEs (Figure S1). Crushers were applied before and after the refocusing pulse to crush the free induction decay signal from the refocusing pulse in case of an imperfect 180° pulse (inhomogeneous B_1). To minimize motion sensitivity, some modifications were made: the slice rewinder gradient was applied directly after the slice excitation pulse, while the phase encoding gradient was applied just prior to the EPI readout train. The motion sensitivity of the crusher gradients around the 180° refocusing pulse is limited, due the relatively slow flow of CSF (around 2-4 mm/s [1]) and the short spacing between both crusher lobes. The shortest used TE was aimed to be shorter than the first non-zero TE for the CSF T_2 mapping sequence, since the SE-EPI sequence has a higher diffusion sensitivity. The longest TE was aimed to be in the same range as the longest TE for the CSF T_2 mapping sequence. Therefore the TEs were heuristically defined according to the following formula: $TE = 240 + 45 \cdot n^2$, for the n^{th} acquisition. This resulted in the following TEs : 240, 285, 420, 645, 960, 1365, 1860, 3120, 3885, and 4740 ms. After the readout a fixed delay time (T_{delay}) was applied. The other parameters are specified at the description of the in vivo measurements.

Phantom experiment

A single slice was acquired with 3x3x6 mm^3 resolution, FOV 240x96 mm^2, sensitivity encoding (SENSE) [2] factor 1, and TR of 15 s, resulting in a T_{delay} of 14.7 s. A series of T_2 maps with increasing through-plane B_0 gradients was acquired to study the effect of diffusion for both sequences for B_1 100%. The following through-plane B_0 gradient strengths were applied by adding this strength to the linear shim term in the user interface: 0, 0.05, 0.1, 0.2, 0.3, and 0.5 mT/m. The acquisition with the highest B_0

gradient was used to study the B_1 dependency of the SE-EPI sequence, similar to the CSF T_2 mapping sequence.

In vivo experiment

The SE-EPI scan was acquired in all seven volunteers, in a single coronal slice (identical slice as the CSF T_2 mapping sequence). The scanning parameters are summarized in Supplementary table S1. Shared parameters were: SENSE factor 2.3 in left-right direction, FOV 240×240 mm^2. The fixed T_{delay} after image acquisition was 14.7 s and TR varied between 15-19s, depending on TE.

Data analysis

Data analysis was identical to the data analysis of the CSF T_2 mapping sequence.

The in vivo ROI masks were made by applying an intensity threshold (25% of the maximum intensity in the scan) to the first echo time for the SE-EPI sequence ($TE_{SE\text{-}EPI}$ = 0.24 s), leading to similar ROIs compared with the CSF T_2 mapping sequence.

For the partial volume assessment only TEs of at least 960 ms were taken into account in the analysis. The minimum TE of 960 ms is shorter than the minimum TE of 1200 ms for the CSF T_2 mapping sequence, since shorter T_2 values were expected to be found for the SE-EPI sequence due to higher diffusion sensitivity.

Results

Phantom measurements

Supplementary figure S2 shows the results of the phantom measurements for the B_1 (Figure S2A) and B_0 gradient (Figure S2B) dependency. For B_1 = 100 ± 2.5% and B_0 gradient = 0 mT/m, the T_2 value obtained with the SE-EPI sequence was 0.96 s (95% CI: [0.86-1.05]). The SE-EPI sequence showed no B_1 dependency, but considerably shorter T_2 values were found for increasing B_0 gradients.

In vivo measurements

In one volunteer the SE-EPI scan at 3T (both resolutions) could not be acquired due to time constraints. A total of 33 SE-EPI scans was acquired, for both field strengths, and the different resolutions. Per scan 3 fits were made, one per ROI, resulting in a total of 99 fits (36 at 3T, 63 at 7T). Based on the strict requirement on minimum R^2, 21 fits were excluded (8 at 3T, 13 at 7T), which is 21% of the total number of fits (22% at 3T, 21% at 7T), see Supplementary table S2 for a detailed overview.

The in vivo results for the SE-EPI scans with resolution 1×1×4 mm^3 are summarized in supplementary Figure S3. At both 3T and 7T the T_2s measured in the periphery were significantly shorter compared to only the lateral ventricles. In all ROIs and for both field strengths, considerably shorter T_2s were measured with the SE-EPI sequence compared to the CSF T_2 mapping sequence. The results for the other resolutions were not significantly different from the data shown here (all data, for both the SE-EPI sequence and the CSF T_2 mapping sequence, is shown in supporting tables S3, S4, and S5).

Partial volume assessment

The results for the additional analysis of peripheral CSF with the longest TEs only are shown in supplementary Figure S4. At 3T, the peripheral CSF T_2 increased with 83 ms at 3T, although this was not significant. At 7T, no difference was observed between the corrected and uncorrected peripheral CSF T_2.

The results for this analysis for the phantom data resulted in shorter T_2 values (Supplementary figure S5). This T_2 shortening was larger for larger B_0 gradients.

Discussion

For the SE-EPI sequence the peripheral $T_{2,CSF}$ was significantly shorter than the ventricular $T_{2,SCF}$ at both 3T and 7T.

B_1 and B_0 dependency

In the phantom measurements no B_1 dependency was found for the SE-EPI sequence, similar to the CSF T_2 mapping sequence, as shown in Supplementary figure S2. The measurements with an increasing through-plane B_0 gradient resulted in shorter T_2 values for larger B_0 gradients. Only a relatively small gradient was needed to find shorter T_2 values for the SE-EPI sequence, while a much larger gradient was needed to find shorter T_2 values for the CSF T_2 mapping sequence (shown in Figure 3B). This can be explained by the longer echo spacings compared to the CSF T_2 mapping sequence, which increases the sensitivity for diffusion [3]. Higher diffusion sensitivity for the SE-EPI sequence is also apparent from the analysis including only the longest TEs: shorter T_2 values were obtained for the SE-EPI sequence when only the longest echo spacings (longest TEs) were included. In contrast, the CSF T_2 mapping sequence showed similar results when only the longest TEs were included, for all B_0 gradient strengths. The difference in diffusion sensitivity of both sequences, is further illustrated by the relative difference in b-value for both sequences which can be readily computed from the echo spacing and the number of refocusing pulses [4]: the b-value of the SE-EPI sequence is 20 to 986 times larger compared with the CSF T_2 mapping sequence, for TEs 600-4800 ms, respectively. The difference in diffusion sensitivity is also visible in the different behavior of the long TE analysis on the phantom measurements. For the SE-EPI a shorter T_2 is measured if only long TEs (with stronger diffusion weighting) is used, but this is not the case for the CSF T_2 mapping sequence (compare Figure 6 with supplementary Figure S5). The difference in diffusion sensitivity is also visible in the different behavior of the long TE analysis on the phantom measurements. For the SE-EPI a shorter T_2 is measured if only long TEs (with stronger diffusion weighting) is used, but this is not the case for the CSF T_2 mapping sequence (compare Figure 6 with supplementary Figure S5).

Partial volume effects

Partial volume correction showed a relatively small T_2 increase (approximately 80 ms) at 3T, but this was not significant. At 7T the T_2 values did not change. This suggests that for the SE-EPI sequence the observed T_2 difference between ventricular and peripheral CSF is (predominantly) not caused by partial volume effects. However, the T_2 values measured with this sequence are much shorter compared to

the CSF T_2 mapping sequence, probably due to its high sensitivity for diffusion and flow. If the partial volume effect in the CSF T_2 mapping sequence is indeed caused by arterial blood or relatively free water in the outer rim of the cortex, the diffusion sensitivity of the SE-EPI may decrease the sensitivity for partial volume effects from this compartment. Alternatively, it could be that the microscopic gradients around the (venous) vasculature at the brain surface induce a shorter T_2 due to the diffusion sensitivity of the SE-EPI sequence, and that this effect cannot be corrected for by choosing longer TEs.

Peripheral versus ventricular CSF T_2 and field strength dependence

The T_2 difference between peripheral and ventricular CSF was 517 ms at 3T, and 160 ms at 7T, a relative difference of 40% and 26% compared to the T_2 in the lateral ventricles. After partial volume correction, the T_2 difference decreased to 433 ms for 3T, a difference of 33% relative to the ventricular CSF T_2, and was unchanged at 7T. Thus, a much larger T_2 difference between peripheral and ventricular CSF was found compared with the CSF T_2 mapping sequence. The T_2 difference at 3T can be partly explained by the larger B_0 gradient in the periphery, but at 7T the B_0 gradients are similar B_0 gradients were found for all ROIs. Furthermore, overall shorter T_2 values were found compared with the CSF T_2 mapping sequence. The SE-EPI sequence is more sensitive to flow and diffusion than the CSF T_2 mapping sequence, which uses multiple refocusing pulses with a fixed echo spacing that is shorter than the shortest TE used in the SE-EPI sequence. The higher flow and diffusion sensitivity of SE-EPI might (partly) cause the larger T_2 difference between peripheral and ventricular CSF. The CSF flow in the periphery is lower compared to the ventricles and cannot explain a shorter peripheral T_2, but diffusion effects around the blood vessels on the cortex may be relatively strong. Since the ventricular walls are not covered with blood vessels, diffusion effects may be smaller in the ventricles in areas away from the choroid plexus at the base of the ventricles. Based on Kiselev, et al. [5], the level of signal dephasing due to diffusion around blood vessels is larger at 7T compared to 3T. This would imply a larger difference between peripheral and ventricular T_2 at 7T, contrary to our observations. It is conceivable, however, that the relative contribution of macroscopic field inhomogeneity to diffusion related T_2 shortening is larger at 7T than at 3T for the SE-EPI T_2 mapping, which could partially mask

regional differences in microscopic field inhomogeneity. This is, however, not supported by the measured B_0 gradients from the B_0 maps that were acquired in vivo. As we used image based third order shimming at 7T, the shimming at the periphery seemed to be better than the shimming at 3T, which was linear shimming.

Limitations

The SE-EPI sequence resulted in different T_2s compared with the CSF T_2 mapping sequence, partly due to a different sensitivity to e.g. flow and diffusion effects. The effects of these confounding factors on the observed T_2 were not studied thoroughly in this work.

Moreover, for the phantom measurements with increasing B_0 background gradient, the acquired signal decay profile showed some deviation from a single exponential decay profile due to relatively stronger diffusion effects for longer TEs. For the in vivo data however, the acquired signal decay only showed minor deviation from a single exponential decay profile. Some in vivo scans were excluded based on the minimum R^2 of 0.99, this was mainly due to motion and/or the presence of flow voids in the data.

Finally, for the SE-EPI sequence at 7T, the measured peripheral CSF T_2 was 450 ms. For the partial volume correction a minimum TE of 960 ms was used, almost double the CSF T_2. This may decrease the sensitivity for small T_2 changes.

References

1. Sweetman B, Linninger AA (2011) Cerebrospinal fluid flow dynamics in the central nervous system. Ann Biomed Eng 39:484–496.

2. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P (1999) SENSE: Sensitivity encoding for fast MRI. Magn Reson Med 42:952–962.

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4. Carr H, Purcell E (1954) Effects of Diffusion on Free Precession in Nuclear Magnetic Resonance Experiments. Phys Rev 94:630–638.

5. Kiselev V, Posse S (1998) Analytical model of susceptibility induced MR signal dephasing in a microvascular network. Proc. Intl. Soc. Mag. Reson. Med. p 1397

Supplementary tables

Supplementary table S1: Scan parameters

Scan parameters used for the in vivo experiments for the SE-EPI sequence

	Resolution	$TE_{readout}$ [ms]	EPI factor	BW (phase/freq) [Hz/voxel]	Scan dur. [min]
3T	1×1×4	240-4740 [1]	105	8.3 / 978	3:30
	3×3×6	240-4740 [1]	67	23.7 / 1806	3:30
7T	1×1×2	240-4740 [1]	107	8.5 / 1103	3:30
	1×1×4	240-4740 [1]	107	8.5 / 1103	3:30
	3×3×6	240-4740 [1]	37	56.3 / 2626	3:30

[1] The used TEs were: 240, 285, 420, 645, 960, 1365, 1860, 2445, 3120, 3885, 4740 ms

Supplementary table S2: Number of excluded fits

Number of acquired scans and performed T_2 fits and the number of excluded T_2 fits per ROI, for the SE-EPI sequence

		Scans (fits)	**Excluded fits**		
			Lateral ventricles	*Fourth ventricle*	*Periphery*
3T	1×1×4	6 (18)	1	1	0
	3×3×6	6 (18)	1	5	0
Total		*12 (36)*	*2*	*6*	*0*
7T	1×1×2	7 (21)	0	2	0
	1×1×4	7 (21)	1	1	1
	3×3×6	7 (21)	3	4	1
Total		*21 (63)*	*4*	*7*	*2*

Supplementary table S3: In vivo results, lateral ventricles

T_2, B_1, and B_0 values for the lateral ventricles, and the ROI sizes and number of included fits, n, for both the CSF T_2 mapping sequence (T_2-prep) and the SE-EPI sequence

			T_2 [s] median (mean±std)	**B_0 gradient [mT/m] median (mean±std)**	**B_1 [%] median (mean±std)**	**ROI size [mm^2] median (mean±std)**	**n**
3T	T_2-prep	1×1×4	2.03 (1.99 ± 0.16)	0.025 (0.029 ± 0.016)	109 (109 ± 2)	122 (128 ± 85)	7
		3×3×6	1.96 (2.02 ± 0.10)	0.032 (0.034 ± 0.017)	111 (111 ± 1)	54 (68 ± 54)	5
	SE-EPI	1×1×4	1.28 (1.30 ± 0.11)	0.024 (0.023 ± 0.004)	108 (108 ± 2)	127 (148 ± 101)	5
		3×3×6	1.13 (1.16 ± 0.24)	0.029 (0.036 ± 0.023)	109 (109 ± 2)	54 (65 ± 57)	5
7T	T_2-prep	1×1×2	1.07 (1.12 ± 0.17)	0.059 (0.063 ± 0.028)	110 (108 ± 8)	98 (103 ± 95)	7
		1×1×4	1.05 (1.04 ± 0.07)	0.068 (0.066 ± 0.027)	111 (110 ± 5)	87 (83 ± 54)	6
		3×3×6	1.06 (1.04 ± 0.07)	0.062 (0.069 ± 0.034)	113 (110 ± 9)	59 (63 ± 55)	6
	SE-EPI	1×1×2	0.64 (0.66 ± 0.13)	0.057 (0.066 ± 0.038)	110 (110 ± 7)	123 (115 ± 96)	7
		1×1×4	0.61 (0.65 ± 0.12)	0.055 (0.064 ± 0.034)	111 (109 ± 8)	90 (111 ± 110)	6
		3×3×6	0.55 (0.59 ± 0.15)	0.068 (0.076 ± 0.049)	110 (109 ± 11)	54 (65 ± 50)	4

Supplementary table S4: In vivo results, fourth ventricle

T_2, B_1, and B_0 values for the fourth ventricle, and the ROI sizes and number of included fits, n, for both the CSF T_2 mapping sequence (T_2-prep) and the SE-EPI sequence

			T_2 [s] median (mean±std)	**B_0 gradient [mT/m] median (mean±std)**	**B_1 [%] median (mean±std)**	**ROI size [mm^2] median (mean±std)**	**n**
3T	T_2-prep	1×1×4	2.08 (2.04 ± 0.16)	0.028 (0.024 ± 0.009)	112 (110 ± 5)	75 (86 ± 29)	6
		3×3×6	1.99 (1.97 ± 0.19)	0.029 (0.023 ± 0.012)	112 (110 ± 5)	14 (20 ± 13)	6
	SE-EPI	1×1×4	1.30 (1.25 ± 0.32)	0.027 (0.024 ± 0.011)	112 (110 ± 5)	79 (84 ± 26)	5
		3×3×6	1.47 (1.47 ± 0)	0.004 (0.004 ± 0)	100 (100 ± 0)	27 (27 ± 0)	1
7T	T_2-prep	1×1×2	1.12 (1.14 ± 0.21)	0.049 (0.049 ± 0.021)	91 (86 ± 13)	58 (58 ± 24)	6
		1×1×4	0.96 (0.96 ± 0.06)	0.056 (0.057 ± 0.016)	96 (89 ± 18)	60 (64 ± 30)	4
		3×3×6	1.04 (1.14 ± 0.28)	0.051 (0.047 ± 0.014)	92 (93 ± 2)	18 (21 ± 14)	3
	SE-EPI	1×1×2	0.75 (0.74 ± 0.09)	0.042 (0.044 ± 0.016)	94 (92 ± 9)	52 (56 ± 31)	5
		1×1×4	0.61 (0.62 ± 0.15)	0.058 (0.052 ± 0.020)	94 (88 ± 14)	43 (52 ± 32)	6
		3×3×6	0.73 (0.73 ± 0.08)	0.058 (0.047 ± 0.026)	92 (91 ± 9)	18 (18 ± 0)	3

Supplementary table S5: In vivo results, periphery

T_2, B_1, and B_0 values for the periphery, and the ROI sizes and number of included fits, n, for both the CSF T_2 mapping sequence (T_2-prep) and the SE-EPI sequence. a) significant vs lateral ventricles, b) significant vs fourth ventricle

			T_2 [s] median (mean±std)	**B_0 gradient [mT/m] median (mean±std)**	**B_1 [%] median (mean±std)**	**ROI size [mm^2] median (mean±std)**	**n**
3T	T_2-prep	1×1×4	1.67 (1.61 ± 0.13) [a,b]	0.129 (0.194 ± 0.118)	85 (86 ± 4)	632 (664 ± 244)	7
		3×3×6	1.59 (1.60 ± 0.12) [a,b]	0.094 (0.150 ± 0.143)	87 (87 ± 4)	1161 (1103 ± 329)	7
	SE-EPI	1×1×4	0.76 (0.74 ± 0.10) [a]	0.143 (0.187 ± 0.111)	85 (85 ± 3)	818 (774 ± 245)	6
		3×3×6	0.74 (0.72 ± 0.10) [a]	0.114 (0.173 ± 0.123)	86 (86 ± 3)	1283 (1248 ± 352)	6
7T	T_2-prep	1×1×2	0.93 (0.94 ± 0.10) [b]	0.062 (0.067 ± 0.014)	85 (84 ± 7)	421 (456 ± 119)	7
		1×1×4	0.89 (0.92 ± 0.10)	0.061 (0.066 ± 0.014)	85 (85 ± 7)	484 (493 ± 109)	7
		3×3×6	0.91 (0.93 ± 0.10)	0.074 (0.076 ± 0.015)	85 (85 ± 6)	936 (928 ± 224)	7
	SE-EPI	1×1×2	0.46 (0.46 ± 0.08) [a,b]	0.077 (0.080 ± 0.031)	86 (86 ± 8)	501 (493 ± 119)	7
		1×1×4	0.45 (0.45 ± 0.08) [a]	0.080 (0.081 ± 0.028)	88 (88 ± 7)	462 (471 ± 122)	6
		3×3×6	0.43 (0.45 ± 0.08)	0.077 (0.075 ± 0.015)	86 (86 ± 5)	684 (720 ± 207)	6

Supplementary figures

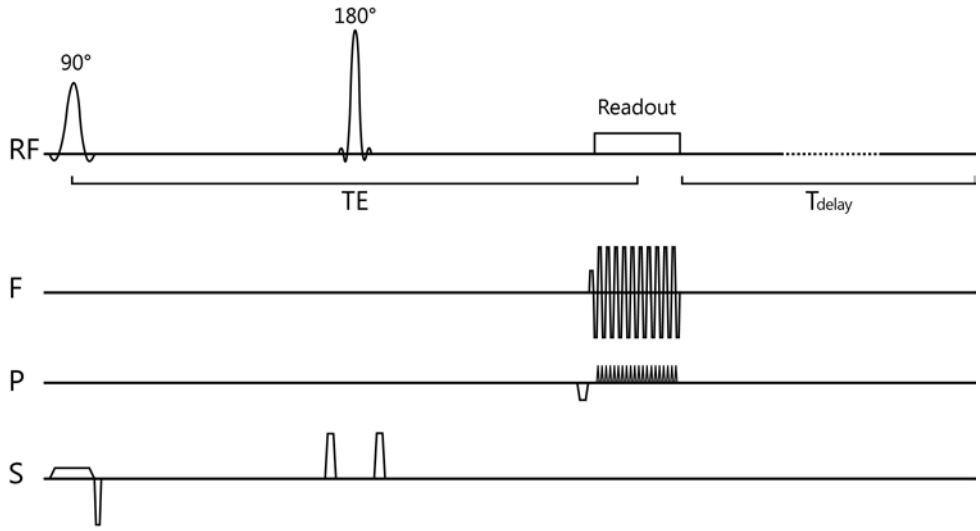

Figure S1 Single echo SE-EPI pulse sequence. For T_2 mapping, the echo time TE was varied. The applied RF pulses are shown on the RF axis, the applied gradients are shown on the frequency (F), phase (P), and slice (S) encoding axes

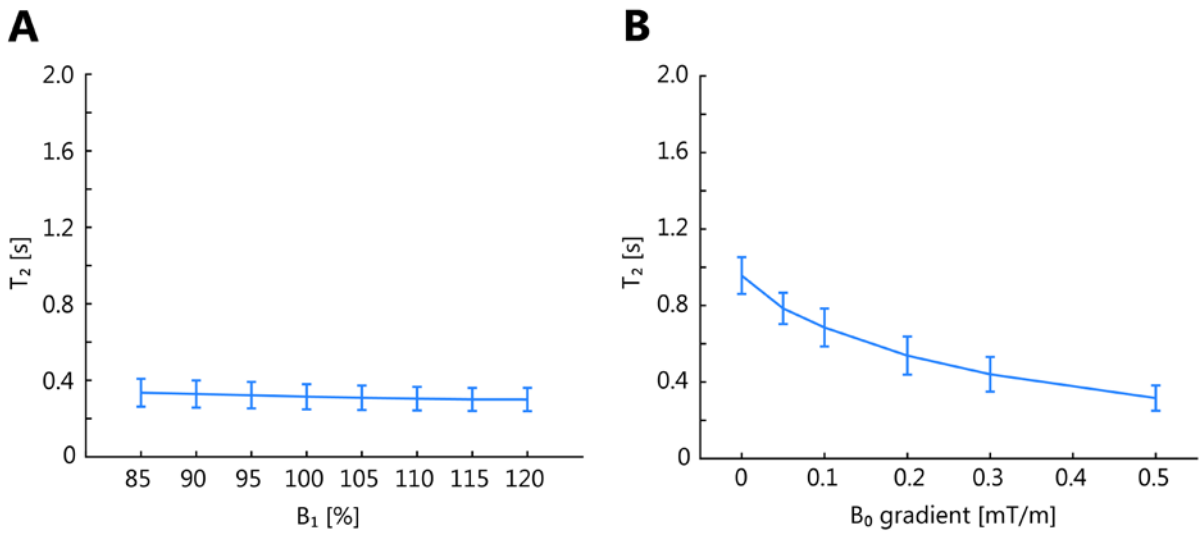

Figure S2 Results of the phantom measurements for the B_1 (A) and B_0 gradient dependency (C), showing the fitted T_2s for different B_1s and through-plane B_0 gradient strengths, respectively. The error bars show the 95% confidence interval of the fitted T_2s. The SE-EPI sequence shows overall shorter T_2s than the CSF T_2 mapping sequence. The SE-EPI sequence is insensitive to B_1, but shows shorter T_2 values for increasing B_0 gradient strengths

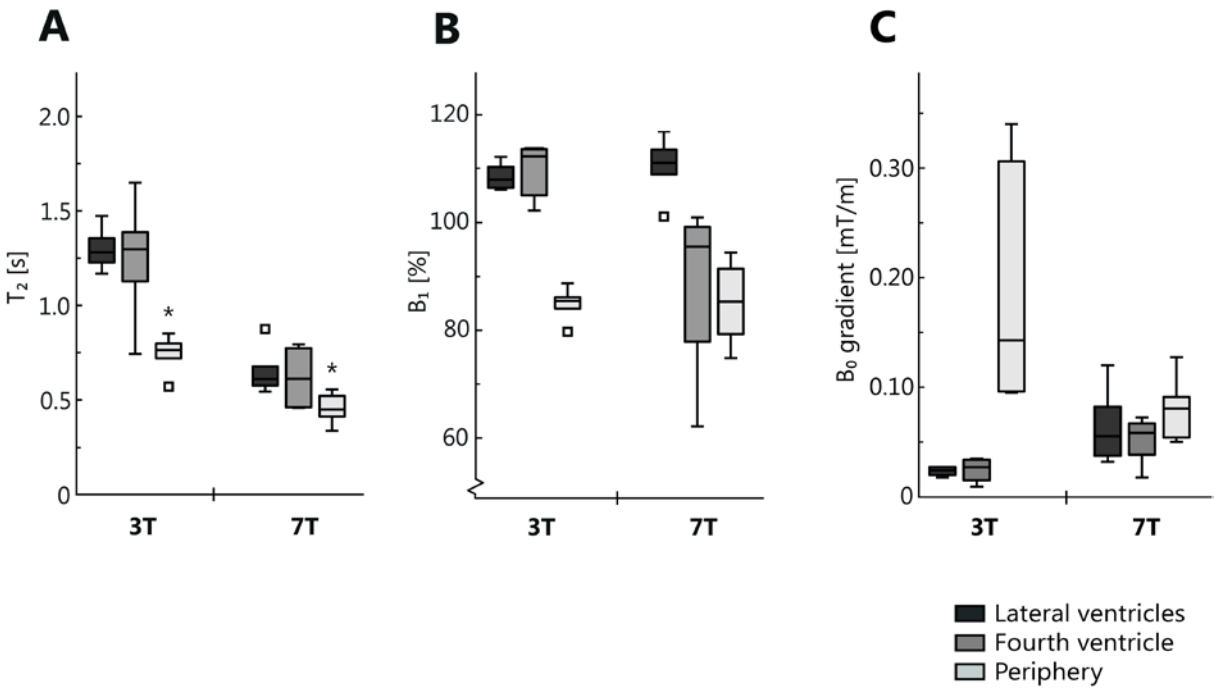

Figure S3 In vivo results: T_2 (A), B_1 (B), and B_0 gradient (C) values for the three different ROIs. Outliers are represented by a square symbol. Significant differences (indicated with the grey asterisk symbol) were found between the periphery and the lateral ventricles for the SE-EPI sequence, at both field strengths (indicated using the asterisk symbol)

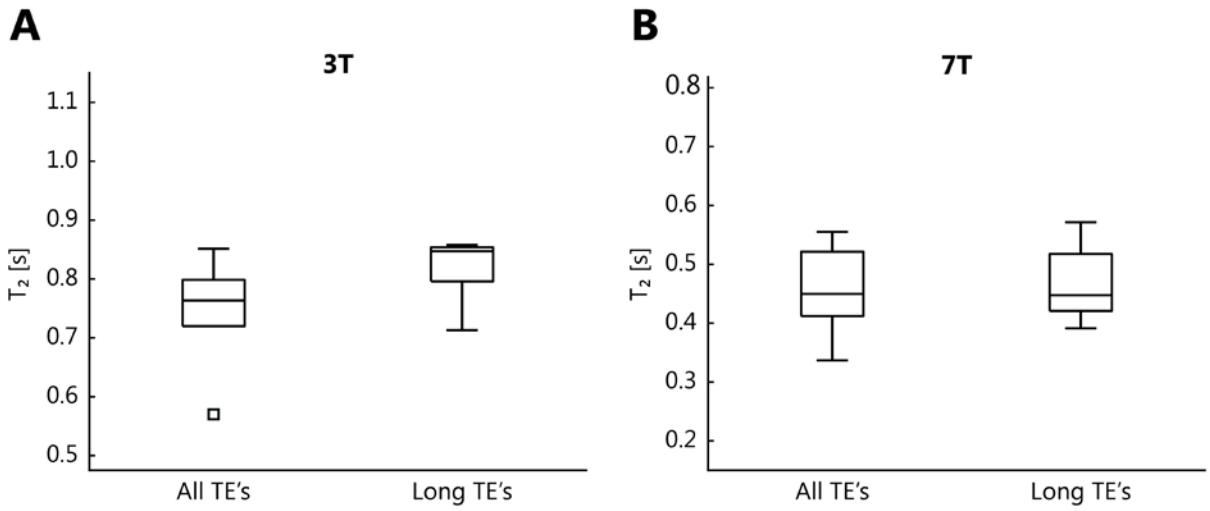

Figure S4 T_2 values of peripheral CSF, resulting from the use of only the longest TEs, compared to the original analysis. Outliers are represented by a square symbol. For the SE-EPI sequence the T_2 increased only at 3T, but this was not significant

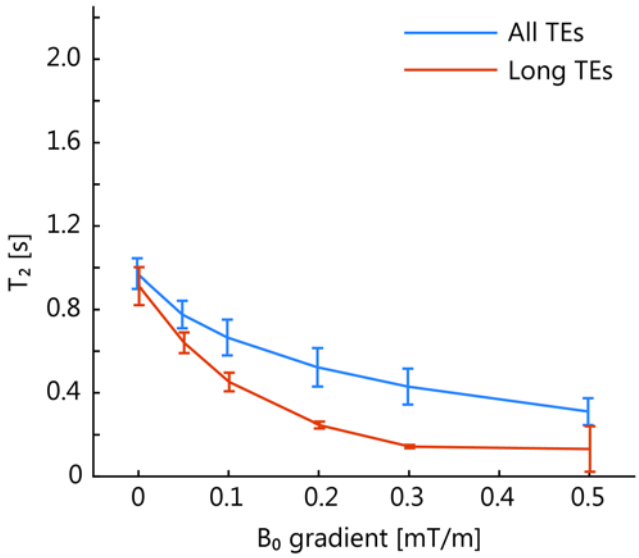

Figure S5 T_2 values of the phantom, resulting from the use of only the longest TEs (orange), compared to the original analysis (blue). For the SE-EPI sequence the T_2 values were shorter for the analysis using only the longest TEs. The difference increased for an increasing B_0 gradient