# Improved T1 relaxometry with NMR field probes: Demonstration of contrast agent characterization

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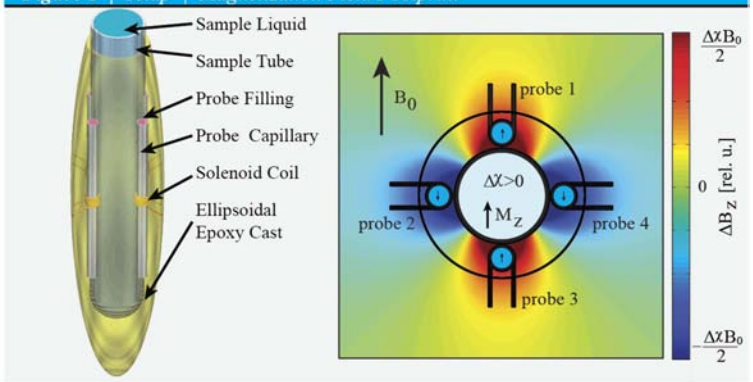
**Introduction.** NMR field probes have recently been demonstrated to permit the direct observation of longitudinal nuclear magnetization and thus highly accurate assessments of $T_1$ relaxation [1]. This capability is based on the fact that a nuclearly polarized sample exhibits a magnetic field around it that scales with its magnetization. This field is exceedingly small (about 30 nT for water at 7 T). However, it can be detected using very sensitive NMR field probes [1]. For cylindrical sample geometry, the field footprint is that of a dipole and consists of four lobes with equal field amplitude but alternating sign. Placing one NMR field probe in each lobe and using a signed summation of the measured fields yields a net value proportional to the sample magnetization while suppressing external fluctuations. A good measure of the quality of such data is $\xi = |\Delta B_0|/\sigma_B$, where $|\Delta B_0|$ denotes the inversion amplitude and $\sigma_B$ the precision of the field measurement. In this work, $\xi$ is increased 17 times compared to the previous publication. The added sensitivity is exploited for a first demonstration of studying the relaxivity of a contrast agent by direct $T_1$-relaxation measurements.

*Figure 1 | Setup | Magnetization Field Footprint*




**Methods.** *Minimizing $\sigma_B$:* Since the field measurement precision for static magnetic fields using NMR field probes depends on the overall sampling time like $\sigma_B \sim T_{obs}^{-3/2}$ [2], to obtain highest SNR, the probe's FID life time has to be maximized within the constraints given by the application (i.e. desired temporal resolution, $T_2$*-decay). Because in this work the expected field dynamics are fairly slow, the $T_2$ of the NMR field probe (hexafluorobenzene ($C_6F_6$), 2.2 mm inner diameter) was chosen to be 20 ms, allowing a $T_{obs}$ of 40 ms before $T_2$*-induced dephasing occurs. *Maximizing $|\Delta B_0|$:* The efficiency of the sample inversion can be optimized using adiabatic pulses. Although these pulses can be designed to be robust against $B_0$-inhomogeneities, high-bandwidth pulses usually mean longer pulse duration which is typically not desirable. The setup was built from epoxy, whose magnetic susceptibility was matched to that of the copper wire used to wind the field probe solenoids [2]. By statically shimming the setup through susceptibility matching, the $B_0$-inhomogneities inside the sample volume could be reduced to less than 100 Hz and a 1.5 kHz bandwidth inversion pulse proved sufficient. This new geometry also improved the homogeneity of the $B_0$-field at the field probe positions, leading to more benign $T_2$*-decay. *Dynamic setup magnetization:* Since the $^1$H-nuclei of the epoxy setup are affected by the inversion pulse applied to the sample, the setup $T_1$ relaxation confounds the sample $T_1$ determination. Three approaches were tried to tackle this issue: (i) A bi-exponential fit was applied to fit $T_{1,\,sample}$ and $T_{1,\,setup}$. (ii) In a sesqui-exponential fit the $T_{1,\,setup}$ – as determined in a calibration step – was kept fixed. (iii) A mono-exponential fit for $T_{1,\,sample}$ is applied to the relaxation curve where the pure setup relaxation curve was subtracted; the latter was obtained in a calibration scan where the sample liquid was replaced by $D_2O$ (neither containing $^1$H, nor $^{19}$F).

**Experiments**. $T_1$ of a water sample and of a Dotarem (Guerbet GmbH, Sulzbach, Germany) in water dilution series were measured. All experiments were performed in a 7 T Achieva MR scanner (Philips Healthcare, Cleveland, USA). Simulations were performed to assess the influence of non-thermal noise on the fitted relaxation values.

**Results.** *Experiments:* A standard deviation of the field measurement of 50 pT was reached. For a water sample a $|\Delta B_0|$ of 13.8 nT was observed, which compares well to the expected maximum value of 14 -16 nT obtained by numerical simulation. A single shot longitudinal relaxation curve for pure water at 22°C is shown (Fig. 2). Bi-exponential fitting (ii.b), where $T_{1,\,setup}$ was kept fix to 1.075 s, resulted in a water $T_1$-value of 3.12 ± 0.04 s. The RMS error of the fit (57 pT) corresponds nicely with the reported field resolution. Fig. 3 shows the Dotarem in water dilution series. These single-shot curves were fitted mono-exponentially using the fitting approach (iii). The 95% confidence interval of the fit is indicated. The initial overshoot of the 0.6 mM concentration relaxation curve (turquoise) is due to setup $T_1$-relaxation, adding up with a negative sign due to its geometry factor relative to the field probe positions. *Simulations:* To compare the three fitting approaches, a $\Delta B_0(t)$ relaxation curve with $T_{1,\,sample}$ = 3 s and $T_{1,\,setup}$ = 1 s was simulated and real-valued noise added. The fitted $T_{1,\,sample}$ were 3.026/3.003/3.002 ± 0.04/0.02/0.015 s (95% confidence interval) respectively for methods (i/ii/iii). The simplicity of approach (i), requiring no calibration, is punished with the highest uncertainty, while the elaborate calibration of approach (iii) results in the smallest expected error. Once the $T_{1,\,sample}$ / $T_{1,\,setup}$ ratio approaches 1, the picture changes and approach (iii) is the only viable method. For this reason it is used for the dilution series, where any $T_{1,\,sample}$ must be expected.

*Figure 2 | Single Shot Data | Exponential Fit | Residuals*

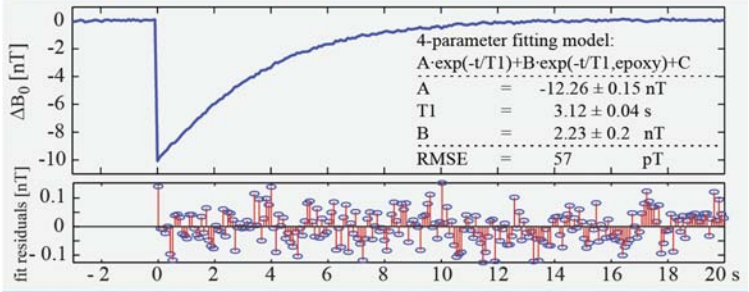
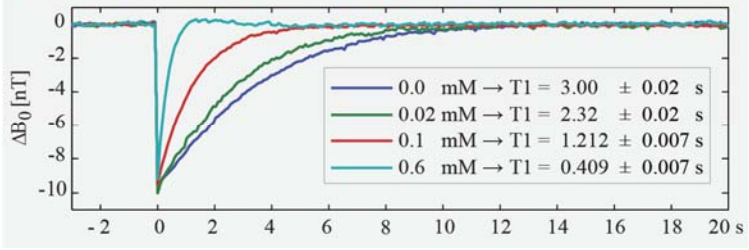



*Figure 3 | Dotarem Dilution Series | Single Shot Data | Fit*




**Discussion and Conclusion.** Improved static shimming of the novel measurement setup enabled a prolonged observation duration per field probe readout as well as a near-perfect inversion. Thus a field sensitivity of 50 pT was reached, a nearly ten-fold improvement compared to [1]. Considering epoxy $T_1$-relaxation, three fitting approaches were studied, trading-off ease of implementation (calibration) versus fit confidence interval. A calibration was proposed in combination with a fitting method, which allows for $T_{1,\,sample}$ determination over a large range, including values in the vicinity of $T_{1,\,setup}$. With these extensions, the method opens up the possibility of charting contrast agent relaxivities in function of their concentration, temperature, pH, in water or blood samples. The speed of the method (one $T_1$-measurement per ≈ 5 $T_1$) also enables the study of temporal dynamics of $T_1$, e.g., in biological samples.

**References. [1]** Gross et al., Proc. ISMRM 20:378 (2012). **[2]** De Zanche et al., MRM 60:176 (2008).