Contrast Reagent Detection Sensitivity Increases with B0: 3T and 7 T Comparisons of Human Head

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Introduction: Contrast reagents (CR) find widespread use in MRI with estimates indicating their application in as many as 40% of all clinical studies. Although most clinical studies are currently performed at 3T and below, ultra-high field $\mathbf{B_0}$ MRI instruments have important advantages, particularly with regard to increased signal/noise and spatial resolution, and unique image contrast. An important consideration in ultra-high field MRI relates to CR detection sensitivity. It is well known that the longitudinal relaxivity, r_1, of low molecular weight gadolinium chelates, decrease with increasing $\mathbf{B_0}$ - which by itself leads to reduced detection sensitivity.[1] However, intrinsic tissue longitudinal relaxivity (r_{1M}, principally due to the macromolecular volume fraction) also decreases with increasing $\mathbf{B_0}$, and to an even greater extent than CR r_1 in the clinically relevant field $\mathbf{B_0}$ range.[2] Taken together, these considerations suggest that, just due to relaxivity properties alone, CR detectability should increase with $\mathbf{B_0}$. Based on literature values for the field dependence of tissue longitudinal and cell-free $GdDTPA^{2-}$ relaxivities, the expected $\mathbf{B_0}$-dependence of CR detection sensitivity (which is proportional to r_1/R_{10}) is plotted in **Figure 1**. This behavior is supported by several reported observations.[3-4] The purpose of this study was to quantify the detection sensitivity of a low molecular weight gadolinium based CR at 3T and 7T in human head tissue.

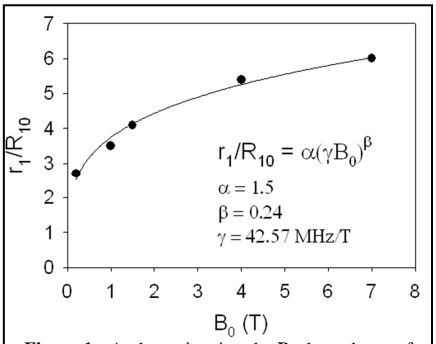
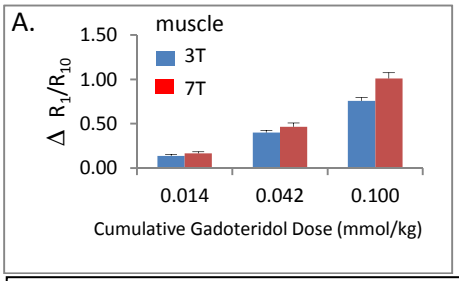


Figure 1. A plot estimating the $\mathbf{B_0}$-dependence of CR detection sensitivity. Filled circles represent the ratio of CR relaxivity to cerebral gray matter ^1H_2O R_1.[1,2] The solid curve represents the power law function with parameters given.

Methods: Twelve subjects provided informed consent and were studied at 3T and 7T using a dynamic contrast enhanced MRI protocol. All 3T data were collected on a Siemens TIM Trio using a body coil transmitter and a 12-channel phased array head coil receiver. All 7T data were collected on a Siemens 7T using an 8-channel phased array transmit/receive RF coil. Four sets of whole brain MPRAGE images were acquired at inversion times (TI) of 300, 900 and 2000 ms; and without an inversion pulse [FOV: 160 mm x 192 mm x 256 mm, matrix: 64x96x256, TE2.1/TR2500/FA8, total acquisition time, 4 x (2 min)]. R_1 maps were generated from the MPRAGE image sets by solving the Bloch equations on a voxelwise basis. Identical qR_1 acquisition sequences were applied at 3T and 7T, typically within one week in random order and included a three-injection CR administration. Gadoteridol was administered at a total dose of 0.1 mmol/kg through the antecubital vein.

Results and Discussion: **Figure 2** compares results for two tissue types; muscle and white matter (WM), which differ markedly in CR extravasation behavior. Figure 2A shows the normalized difference for ^1H_2O R_1 (i.e. $\Delta R_1/R_{10} = (R_{1CR} - R_{10})/R_{10} = r_1[CR]/R_{10}$; where R_{1CR} is the tissue ^1H_2O R_1 value 5 minutes after a specific CR dose) from bilateral *temporalis* muscle regions-of-interest (ROI; cumulative doses indicated on abscissa of Fig 2). The blue bars and the red bars measure the group average normalized ΔR_1 values at 3T and 7T, respectively. At each dose the 7T $\Delta R_1/R_{10}$ value exceeds the paired 3T value ($p < 0.001$) by an amount increasing by dose. An analogous plot is provided for large WM ROIs located bilaterally in the *centrum semiovale* (CSO) (Fig. 2B) also shows greater CR detection sensitivity at 7T compared to 3T ($p < 0.003$). It is important to appreciate that the total sensitivity increase includes not only relaxation property differences, which we demonstrate are significantly improved at 7T compared to 3T, but also increased base image signal to noise (S/N). Increased 7T S/N improves precision of individual tissue R_1 determinations compared to 3T; here by approximately a factor of 1.6 (see **Figure 3**). It is important to note that the error bars in Fig 2 are largely determined by inter-individual differences. Our results show improved precision of R_1 determination for individuals, although coverage was superior at 3T with the RF coil configurations used in this study. In summary, our results strongly support the view that CR detection improves at 7T compared to 3T. This finding is important for several reasons. Importantly, it allows lower CR doses to be used to achieve the same lesion conspicuity which improves the CR administration safety margin. Also, it allows more precise characterization of tissues demonstrating low extravasation such as most normal brain regions.



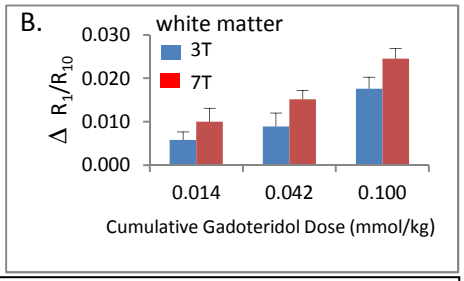


Figure 2. Detection sensitivity of MRI CR in human subjects at 3T and 7T. Subjects were studied using essentially identical MR acquisitions and CR delivery protocols. (**A**) comparison of normalized change in temporalis muscle ^1H_2O R_1 values following three gadoteridol injections (0.014, 0.028, and 0.058 mmol/kg doses; total dose = 0.1 mmol/Kg). For all doses 7T values exceeded those at 3T ($p < 0.001$). The filled bars represent R_1 differences due to $\mathbf{B_0}$ dependence of tissue and CR relaxivities only; contrast to noise differences in base images are not included. (**B**) comparison of normalized change for cerebral white matter ^1H_2O R_1 where CR remains intravascular. Note the much decreased ordinate values in (B) compared to (A). Nevertheless, a significant improvement in CR detectability is realized at 7T compared to 3T ($p < 0.003$).

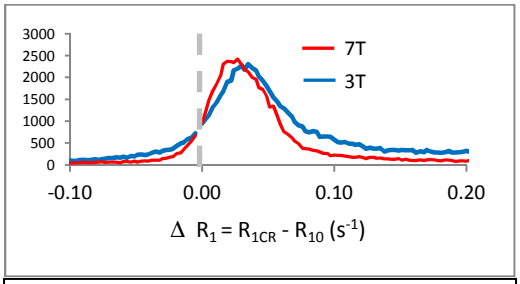


Figure 3. White matter ΔR_1 histogram (post CR – pre-CR) for a single subject at 3T and 7T. Number of voxels in presented on the ordinate axis. The7T histogram has a tighter distribution compared to the 3T; the distribution averages (stdev) are 0.032 (0.030) s^{-1} and 0.027 (0.018) s^{-1} for 3T and 7T, respectively. The fraction of voxels with $\Delta R_1 < 0$ is 12% and 8.5% for 3T and 7T, respectively.

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References: **1.** Rooney, Johnson, Li, Cohen, Kim, Ugurbil, Springer, MRM 57:308-318 (2007). **2.** Aime, Botta, Fasanao, Terreno. Chem. Soc. Rev. 27 :19-29 (1998). **3**. Bolinger, Cecil, Englander, Stolpen. PISMRM 6:232 (1998). **4.** Stehouwer, Klomp, Korteweq, Verkoojen, Luitjen, Mail, van den Bosch, Veldhuis. Magn. Reson. Imag. 29 Oct 2012 (in press).