Probing T_1- and Off-Resonance-Based Signal Enhancements with Gd-DTPA Using Fast Low Angle Positive Contrast Steady-State Free Precession Imaging

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Introduction: Gadolinium-based contrast agents typically generate positive signal enhancement on T_1-weighted (T_1-w) images through direct interaction with water molecules to shorten T_1. T_1-w signal enhancement, as a function of gadolinium concentration ([Gd]), generally increases to a peak value and then decreases as T_2* effects begin to dominate [1]. Pronounced T_2*shortening, particularly at high [Gd], is associated with increased field inhomogeneities originating from an overall shift in magnetic susceptibility in the molecular environment of water protons. This susceptibility shift may induce the far-field protons to precess at slowly varying off-resonant frequencies in space (static-dephasing regime). Recently, a number of methods aimed at selectively visualizing protons in the static dephasing regime have been developed [2-5]. One of these methods is Fast Low Angle Positive-contrast Steady-state free precession imaging (FLAPS) imaging, which is weighted by T_1/T_2 and far field off-resonance shifts [5]. The FLAPS technique takes advantage of the unique spectral response of the steady-state free precession (SSFP) signal with respect to flip angle to generate off-resonance-based positive contrast. We hypothesize that, dependent on paramagnetic agent concentration, FLAPS offers the flexibility to capture both the direct (T_1) and indirect (far field off-resonance) effects as signal enhancements.

Methods: All studies were performed on a 3T Tim Trio scanner (Siemens Medical Solutions, Erlangen, Germany) using a product head coil for signal reception. FLAPS imaging was used to investigate the signal enhancement patterns over a broad range of [Gd] (Gd-DTPA, Magnevist, Berlex, NJ, USA). In order to relate the T_1 enhancements obtained with FLAPS to a relatively pure T_1-w sequence, a fast low-angle shot T_1-w sequence (FLASH) was also prescribed over the full range of [Gd]. Individual acrylic cylindrical phantoms (diameter = 1.59 mm), each containing one of nine gadolinium concentrations (0.0, 0.5, 1, 2, 5, 8, 14, 30, 50 mM) were placed in a water bath perpendicular to the main magnetic field and imaged in the coronal plane using FLASH and FLAPS. Each measurement was repeated 3 times to assess reproducibility. Scan parameters common to FLASH and FLAPS sequences were: $\alpha = 20^o$, $T_R = 7.7$ ms, acquisition time = 3.4 s, and voxel size = 0.4 x 0.4 x 5 mm^3. T_E for FLASH and FLAPS sequences were 3.3 ms (minimum T_E) and 3.85 ms ($T_R/2$), respectively. Contrast-to-noise ratio (CNR) was calculated as (SIe - SIb)/ σ_{air}, where SIe is T_1- or off-resonance–weighted signal enhancement; SIb is background signal, and σ_{air} is the standard deviation of noise. T_1-based signal enhancement was measured as the mean signal intensity of a ROI placed within the cross-section of the cylinder. To measure the off-resonance-based contrast, signal measurements were made outside the cylinder over regions showing positive contrast.

Results: T_1-based contrast (inside cylinder – FLAPSin and FLASHin) rose rapidly and peaked at 8mM with FLASH and FLAPS. FLASH-based contrast outside the cylinder (FLASHout) remained constant and nearly zero throughout the full range of [Gd] studied. FLAPS-based off-resonance contrast (outside cylinder - FLAPSout) rose as [Gd] increased (Figure 1). In particular, it was observed that FLAPS and FLASH produced increasing positive contrast due to T_1 effects for [Gd] < 8 mM. For [Gd] > 8 mM, FLASH and FLAPS produced decreasing T_1-based positive contrast, while over this range FLAPS showed a marked increase in off-resonance-based positive contrast. For [Gd] > 40 mM, only the off-resonance-based positive contrast was visible in FLAPS. A representation from each of these [Gd] regimes is shown in Figure 2.

Discussion & Conclusion: The data confirm our hypothesis that FLAPS imaging can be used to produce signal enhancements from direct (T_1-shortening) and indirect (off-resonance) effects. Within the range of [Gd] investigated here, three regimes of positive contrast can be identified for FLAPS imaging: (a) Regime I, where the T_1-shortening dominates; (b) Regime II, where both T_1 and off-resonance effects are present; and (c) Regime III, where only off-resonance effects mediate positive contrast, as shown in Figure 2. Although the range of [Gd]s that define each of these three regimes is identified for Gd-DTPA, in general the range of [Gd] defining the three regimes may be dependent on the physical properties of the agent, the physical environment of the near and far field protons, and imaging parameters [1,5]. We anticipate that the results here may guide or permit an accurate interpretation of positive contrast imaging studies seeking applications in cellular imaging, contrast angiography, and/or visualization of passive interventional devices [7].

References: [1] Watson AD et al. IN: Stark DD et al. Magnetic Resonance Imaging 1992, p. 374. [2] Cunningham CH, MRM 2005;53:999; [3] Stuber M et al., 13th ISMRM p. 2608.; [4] Mani V et al 2006;55:126 ; [5] Dharmakumar R et al., Phys. Med. Biol. 2006, p. 4201; [6] Chambon C et al. MRI. 1993, p.509; [7] Edelman R et al. 18th MRA Club; p. 32.

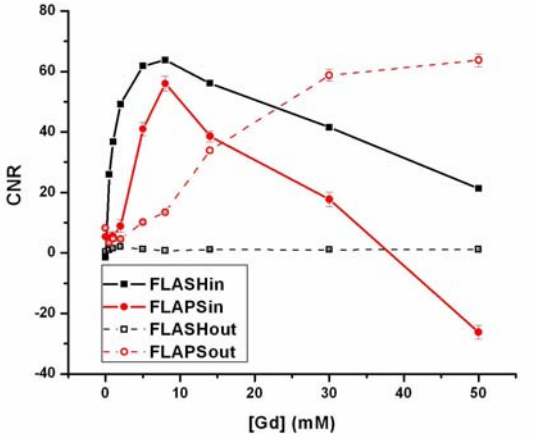

Figure 1. Positive contrast due to T_1 and off-resonance effects as a function of [Gd]. T_1-mediated contrast from FLASH (closed squares) and FLAPS (closed circles) and off-resonance-based positive contrast from FLAPS (open circles) is shown as a function of [Gd]. As T_1-based contrast decreases, off-resonance-based positive contrast increases. CNR is reported as mean +/- standard error.

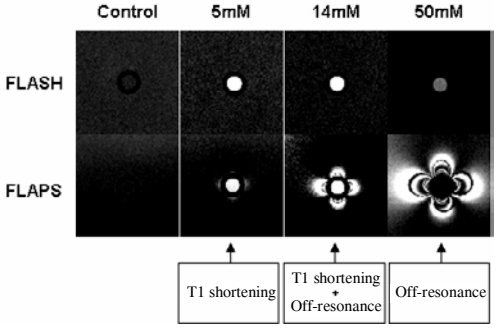

Figure 2. Cross-sectional images of the cylinder filled with increasing gadolinium concentrations (Control (0.0 mM), 5-, 14-, and 50-mM). FLASH images (top row) show only direct effects, while FLAPS images (bottom row) illustrate three regimes of signal enhancement, as described in the text.