

DYNAMICAL EVALUATION OF THE LONGITUDINAL RELAXATION RATE OF BLOOD AFTER ADMINISTRATION OF GADOBENATE DIMEGLUMINE FOR OPTIMIZED SS-MRA

Fabio Tedoldi¹, Cristina Neira¹, Michele Anzidei², Alessandro Napoli², Miles Kirchin³, Fulvio Uggeri¹, Beatrice Cavallo Marincola², Fulvio Zaccagna², Carlo Catalano², and Roberto Passariello²

¹Centro Ricerche Bracco, Bracco Imaging Spa, Colleretto Giacosa, Torino, Italy, ²Department of Radiological Science, University of Rome 'la Sapienza', Rome, Italy,

³Bracco Imaging SpA, Global Medical and Regulatory Affairs, Milan, Italy

Introduction: Gadobenate dimeglumine is a Gd-based chelate that is widely used for contrast enhanced magnetic resonance angiography (CE-MRA) procedures. Although not a dedicated intravascular agent, it interacts weakly and transiently with serum albumin resulting in increased longitudinal relaxivity (r_1) relative to conventional Gd-based contrast agents. Recently, Anzidei et al. (1) have shown that the increased r_1 renders gadobenate dimeglumine suitable for Steady State (SS) CE-MRA and that the additional diagnostic information available on combined first passage (FP) and SS CE-MRA is potentially greater than that on FP alone for both carotid and peripheral CE-MRA. As yet, however, few studies have been performed to optimize the acquisition protocols for CE-MRA with gadobenate dimeglumine. The present investigation aimed to define the optimal flip angle (FA) for gadobenate dimeglumine-enhanced SS MRA and was performed in three distinct phases: 1) *in vitro* optimization of an inversion recovery protocols for dynamical monitoring of the longitudinal relaxation rate R_1 ; 2) *in vivo* dynamical evaluation of R_1 in blood after administration of gadobenate dimeglumine and determination, for different repetition times (TR), of the optimal flip angle for SS MRA ; 3) assessment of the benefits of using a calibrated Ernst Angle in SS MRA of carotid arteries.

Methods: *In vitro optimization:* Phantom studies were performed at 1.5 T using a clinical whole body MR scanner equipped with a transmitting body coil and a receiving head coil. A multi-tubes test phantom was prepared by mixing in different concentration a commercial formulation of 0.5 mol/L gadobenate dimeglumine with a physiological saline solution. The reference standard for the R_1 evaluation was a spin echo (SE) sequence, in which TR was varied between 20 and 10,000 ms to monitor the exponential recovery of the longitudinal magnetization. The inversion recovery fast low angle shot (IR-FLASH) sequence to be subsequently exploited *in vivo* has been tested against the SE for different combinations of flip angle (FA, between 6° and 14°) and inversion time (TI, between 134 and 9,000 ms). *In vivo studies:* 25 patients (17 male, 8 female; age: 54 ± 3 years; range: 48 – 70 years) scheduled for a contrast-enhanced MRI examination for non-vascular indications were enrolled after approval of the Local Institutional Committee of Medical Ethics. All subjects provided written informed consent after having been informed of the potential benefits and contraindications of CE-MRA. On five patients, the optimized IR-FLASH sequence was used to monitor the time evolution of blood R_1 at 1.5 T after administration of gadobenate dimeglumine at 0.1 mmol/kg bodyweight. An optimal FA for angiographic measurement was thereafter derived from the Ernst equation based on experimental values of R_1 previously determined *in vivo*. Steady state CE-MRA examinations of carotid arteries were performed in the remaining 20 subjects by means of a 3D gradient echo sequence in order to evaluate the improved contrast achieved after optimization of the FA for maximal blood signal enhancement.

Results: An ultra-fast IR-FLASH sequence with FA=8° and a properly defined set of TI values was shown to give *in vitro* R_1 determinations in good agreement with those obtained by a routine variable-TR SE sequence. The use of this ultra-fast IR-FLASH sequence *in vivo* allowed the blood signal behavior in the carotid arteries after gadobenate dimeglumine administration to be monitored. R_1 was found to decrease exponentially from 8.7 ± 0.96 s-1 at 30 sec post injection to 3.8 ± 0.24 s-1 at 10 min post injection, in agreement with theoretical predictions based on gadobenate dimeglumine pharmacokinetic data (2) and *in vitro* r_1 relaxivity (3,4). Optimal flip angles, at different TR, for SS angiography with gadobenate dimeglumine, derived according to Earnst equation from our R_1 experimental data are displayed in Fig. 1. Significantly higher blood Signal to Noise Ratio (SNR) was achieved on SS images of carotid arteries acquired using a 3D spoiled gradient echo sequence with TR = 7.5 ms and FA=18° than on corresponding images acquired with a FA=35° as used typically for intravascular blood pool contrast agents (52.5 ± 8.3 vs. 29.5 ± 6.0 ; $p < 0.05$, Mann Whitney U test), as displayed in Fig. 2.

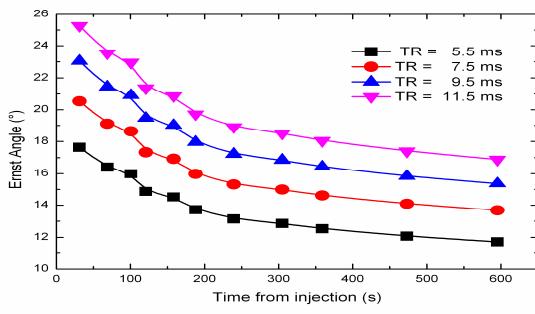


Fig. 1: Ernst Angle versus post injection time calculated for different TR values.

Conclusions: Detailed experimental knowledge of the *in vivo* R_1 behavior of blood after gadobenate dimeglumine injection and appropriate modification of the acquisition parameters have been shown to enable improved signal intensity enhancement on steady-state CE-MRA of the carotid arteries.

References: (1) Anzidei et al., Invest Radiol. 2009; 44:784-792 and Invest Radiol. 2011; 46:307-316. (2) Spinazzi et al., Acad Radiol 1999; 6: 282-291. (3) Pintaske et al., Invest Radiol. 2006; 41:213-221 - erratum in Invest Radiol. 2006; 41:859. (4) Rohrer et al., Invest Radiol 2005; 40:715-724.

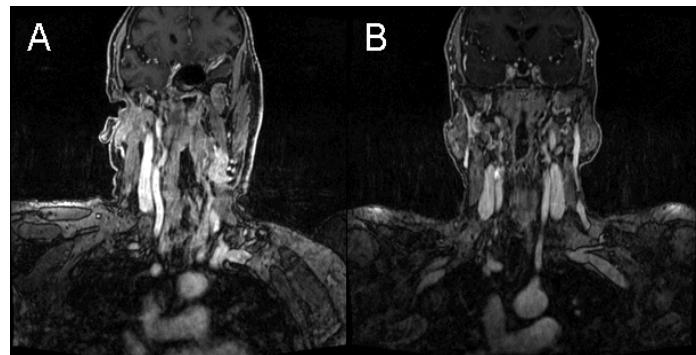


Fig. 2: Comparison between SS images acquired with FA = 18° (A) and FA = 35° (B). In both acquisitions TR was set to 7.5 ms.