

Gd-enhanced MRI after therapeutic ferumoxytol for iron deficiency anemia - An in-vitro study for optimal contrast timing and dose determination.

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Target audience: Practicing radiologists, MR physicists.

Purpose: Ferumoxytol is an injectable compound that has been FDA approved for treatment of iron-deficiency anemia in adult patients with chronic kidney disease. It is usually administered as an initial 510 mg injection followed by a 2nd 510 mg injection three to eight days later. Although a rare occurrence, some of the patients who have received intravenous ferumoxytol may undergo a gadolinium enhanced scan in the initial days after the injection. As the iron in the compound is in the form of a superparamagnetic iron oxide which causes T1, T2 and T2* shortening, and also has a long intravascular half-life, it has been shown to confound the effects of subsequently performed gadolinium enhanced scans (1). The purpose of our study is to determine the concentration of ferumoxytol which will not confound arterial enhancement in subsequent gadolinium enhanced studies and enable us to determine optimal scheduling timing of the MRI study post therapeutic ferumoxytol injection.

Methods: Various concentrations of ferumoxytol and gadolinium were mixed in 10 ml test tubes diluted by normal saline. 3 concentrations of ferumoxytol were used. The first was Cmax (C) which according to literature is approximately 300 micrograms per ml (2). The other two were 150 micrograms per ml (C/2) as expected after one half-life (15 hrs) and 75 micrograms per ml (C/4) as expected after 2 half-lives (30 hrs). 3 concentrations of Omniscan (Gadodiamide) were used based on single (SD), double (DD) and triple (TD) dosing and an arterial volume of distribution in a 70 kg man of 2000 ml (pulmonary + systemic arterial + heart + capillaries). 16 test tubes were composed. These were imaged using a 3T scanner and T1 weighted axial fat-sat images (TE 2.1, TR 4.3 and FS 3) were obtained (Image 1). The signal intensity of various test tubes on the obtained images was analyzed after region of interest placement.

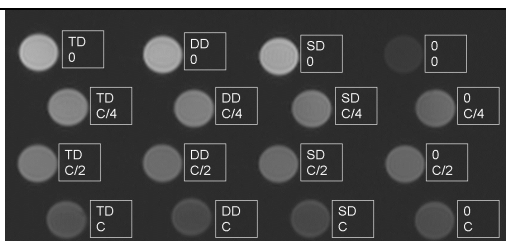
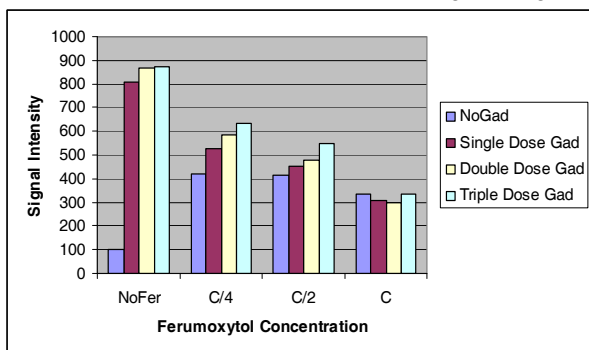


Image 1 – 16 test tubes with various concentrations of ferumoxytol with **C** representing Cmax after two therapeutic injections, **C/2** representing concentration one half-life after Cmax and **C/4** representing concentration two half-lives after Cmax. **SD** represents concentration of gadodiamide after single dose i.e. 0.1 mmol/kg, **DD** after double dose and **TD** after triple dose.

Results: For ferumoxytol concentration at Cmax, there was no significant enhancement noted after single, double or triple dosing of gadodiamide. After one half-life of ferumoxytol, at concentration C/2, there was mean enhancement of 35.4 units or 8.5% after single dosing of gadodiamide, 62.3 units or 15% after double dosing and 130.72 units or 31.4 % after triple dosing. After two half-lives of ferumoxytol, at concentration C/4, there was mean enhancement of 104.5 units or 24.75% after single dosing, 163.2 units or 39.7% after double dosing and 210.9 units or 49.9% after TD. See chart below.



Discussion: High concentration of ferumoxytol can mask enhancement from gadolinium based compounds due to its superparamagnetic effects. The highest dose of ferumoxytol used in this study is based on the Cmax provided on the FDA insert (2,3). However, the FDA insert value was calculated after administration of 2 therapeutic doses on consecutive days. In reality, there is approximately a 3-8 day waiting period between the doses. The Cmax of approximately 300 microgram per ml is almost never seen physiologically. Even if we consider the Cmax of 300 microgram per ml, by just waiting one half-life of 15 hours, we were able to obtain significant enhancement by double dosing (15%) and triple dosing (31%). At two half-lives, there was significant enhancement even after single dosing (24.75%). This data points towards no significant effect of ferumoxytol if gadolinium imaging is performed 1 or 2 days after injection.

Conclusion: Arterial enhancement after gadolinium injection should be visible or discernible by subtraction imaging after waiting one or two half-lives after ferumoxytol injection.

References: 1. McCullough BJ, Kolokythas O, Maki J, Green D. Ferumoxytol in Clinical Practice: Implications for MRI. J Magn Reson Imaging. 2013 Jun;37 (6): 1476-9.doi: 10.1002/jmri.23879.Epub 2012 Oct 23.

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