# WASSR imaging of Iron Oxide Particles at 2.35 and 7T

**J-S. Raynaud[1], A. Lee[1], C. Robic[1], E. Giaccomini[2], I. Raynal[1], P. Robert[1], F. Lethimonier[2], M. Port[1], and C. Corot[1]**
[1]Guerbet Research, Paris, France, [2]Neurospin, CEA, Saclay, France

## Introduction

During the last decade, in addition to standard T2w*, different approaches were designed to detect USPIO such as UTE [1], phase/SWI[2], susceptibility mapping [3], and "positive contrast" strategies [4]. "Positive contrast" imaging based on a single off resonance RF excitation suffers of low sensitivity and miss registrated spatial localization. A way to avoid these drawbacks is the ORS sequence [5], based on a long RF saturation to affect off resonance water diffusible protons. The purpose of this study was to investigate a new sequence initially performed for CEST imaging, WASSR (WAter Saturation Shift Referencing) [6], to combined strong contrast, high sensitivity and quantification. This sequence was evaluated on Iron and Gadolinium based contrast agents in *in vitro* conditions at clinical (2.35T) and research (7T) fields, in spin and gradient echo sequences.

## Material & Methods

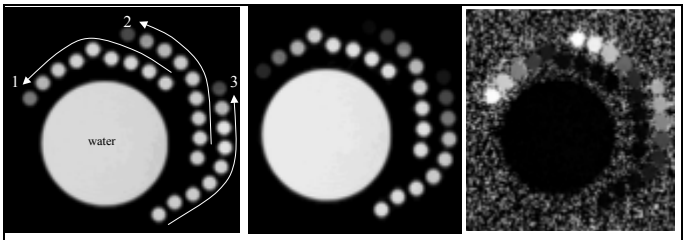
***Phantoms*** *:* USPIO [P904, Guerbet Research], SPIO [Guerbet Research] and Gd emulsions [Guerbet Research] phantoms were realized ranging from 0.3-1000 µM concentrations for USPIO and SPIO and 0.9-2950 µM concentrations for Gd-loaded emulsion.

***MR acquisitions*** *:* Spin echo (MSME) and Gradient echo (GEFC) sequences were carried out on a 7T Pharmascan and a 2.35T BioSpec scanners [Bruker, Ettlingen, Germany]. Twelve 40 ms Gaussian off resonance RF pulses, corresponding to 2-3.5µT B1, were applied. WASSR shift frequency ranged between +/- 600 Hz.

***Post Processing*** *:* Post processing was performed with Matlab software (MathWorks). ORS maps were calculated from "on-off" difference or "off/on" ratio. For WASSR data, signal frequency dependence was fitted by Lorentzian function in order to extract $f_0$ interpolated B0 shift map and half bandwidth frequency map.

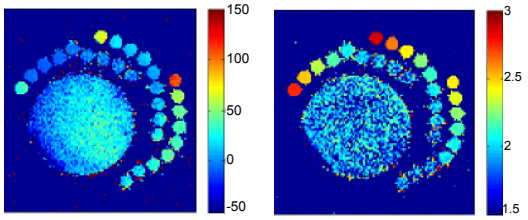
## Results

- As expected, detectability is increasing with the contrast agent concentration either with the simple ORS approach (Fig 1-c) and WASSR approach (Fig 2a-b)
- *Off/On* ORS ratio processing (fig1) avoids relaxation saturation effect at high concentration as opposed to *Off – On* ORS difference (data not shown).
- WASSR half bandwidth maps (corrected to B0 inhomogeneities, ie frequency shift maps $f_0$) demonstrate good contrast and sensitivity even at low contrast agent concentration (fig2-b).
- Extrapolated sensitivity with P904, about 3µM (of Fe), is slightly better at 7T and on spin echo sequence (fig4&5).
- Sensitivity in nano-object is about 300, 75 and 420 pM respectively for P904, SPIO and Gd emulsion. (fig5).




a- "on" at 200 Hz b- "off" c- "off/on" ratio

**Fig 1: ORS imaging at 200 Hz (Ascending concentrations of 1: P904, 2: SPIO, 3: Gd-loaded emulsion)**




a- $f_0$ Frequency shift (Hz) b- ½ bandwidth (Hz)

**Fig 2 : WASSR imaging in the [-600Hz;+600Hz] range**

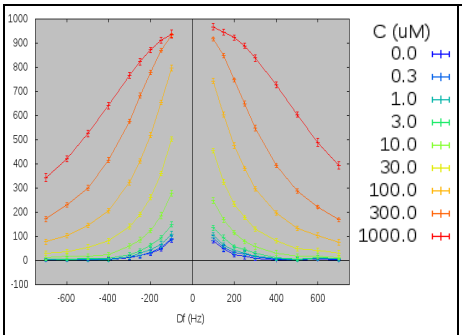



**Fig 3: Example of WASSR fits on P904 at 7T**

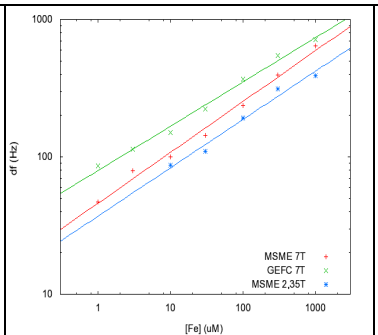



**Fig 4: Frequency shift $f_0$ for P904 in function of Field and sequence**

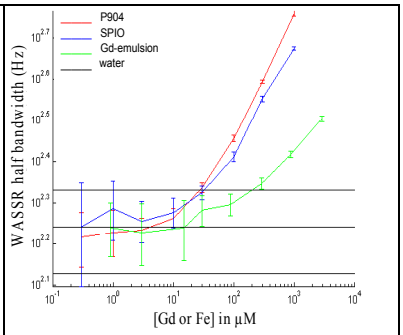



**Fig 5: Detection threshold for sensibility comparison at 2.35 T**

**Conclusion :** ORS/WASSR approach are feasible at both clinical and research magnetic field, but results are slightly better results at 7T with spin echo sequence. Sensitivity, inferior to nM of nano-object, is compatible with *in vivo* acquisition of molecular imaging contrast agent. *In vivo* evaluation which is limited by Specific Absorption Rate and Magnetization Transfert effect still needs to be optimized and evaluated.

**References :** [1] Robson et al., J Comput Assist Tomogr (2003), 27: 825-46. [2] Haacke et al., AJNR (2004), 52:612-18. [3] de Rochefort et al., MRM (2008), 60:1003-09. [4] Liu et al., NMR Biomed. (2008), 21:242-250 [5] Liu et al., NMR Biomed. (2008), 21:242-250 [6] Kim et al., MRM. (2009), 61:1441-50