# Design of Iron Sensitivity Phantom Suitable for Quantitative MRI and Atomic Spectrometry

**C. A. Mallik[1], D. Bellis[2], D. J. Lythgoe[1], R. Santamaria-Fernandez[2], and G. J. Barker[1]**
[1]Centre for Neuroimaging Sciences, Institute of Psychiatry, London, United Kingdom, [2]Laboratory of Government Chemists, Teddington, Middlesex, United Kingdom

## Introduction

There is a growing body of MRI research on the effects of abnormal levels of iron in the brain [1], with several different methods proposed to quantify iron loading, e.g. transverse relaxation [2]; phase [3] and Magnetic Field Correlation (MFC) mapping [4]. Validation of each technique with a phantom of known iron concentrations is useful for determining the sensitivity of different MRI measures. Atomic spectrometry (AS) techniques such as Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS) can be used to determine concentrations of iron in synthetic and histology samples [5]. The aim of this work was to design and manufacture a phantom suitable for both MRI and AS analysis with biologically relevant materials and iron concentrations.

## Methods

Phantom Design and Production: For this preliminary investigative work, concentrations of approximately 0, 100 and 200 μg/g of iron in the form of ferritin were chosen to reflect the range of concentrations typically found in the brain [6]. For AS analysis volumes of less than 1ml are needed. Pilot MR imaging demonstrated that a volume of at least 20ml was required to allow an ROI to be drawn in an artefact free region for the range of techniques investigated. To maintain a homogenous distribution of ferritin throughout the sample a fast-setting thrombin-fibrinogen gel (developed as a tissue-engineered product [7]) was chosen. By altering the relative concentrations of thrombin and fibrinogen, the rate of gelling could be adjusted – an important consideration when casting the increased volumes required for MRI. In addition to the ideal, but costly thrombin-fibrinogen gel base, a set of saline solutions, with the same concentrations of ferritin, were also manufactured. Finally, a set of "iron standards" (solutions typically used in AS assays), were produced to test if they could be used as a surrogate to ferritin. Table 1 describes the components of each type of phantom that were made up to approximately 20mls. Phantoms were housed in a flat-bottomed glass jars, and placed in a bath of maple syrup, which has a short enough $T_2$ to not be detected at the echo times used, and reduces magnetic susceptibility artefacts at jar edges.

| Reagent | Ferritin Gel (%) | Ferritin Solution (%) | Iron Standard Solution (%) |
|---|---|---|---|
| Fibrinogen | 0.33 | - | - |
| Thrombin | 3.03E-05 | - | - |
| Ferritin (max) | 3.19 | 3.07 | - |
| Sodium Azide | 0.06 | - | - |
| Phosphate Buffered Saline | 96.42 | 96.93 | - |
| Iron Standard (max) | - | - | 20.31 |
| Nitric Acid | - | - | 1.00 |
| Water | - | - | 78.69 |
| Total | 100.00 | 100.00 | 100.00 |

Table 1. Constituent phantom parts expressed as % of total mass in manufacturer supplied form

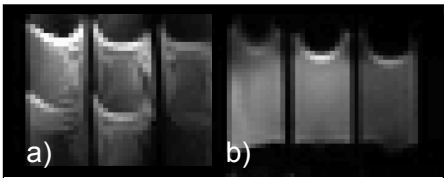


Figure 1. Example MFC acquired images (symmetric spin echo) a) ferritin gels in air b) ferritin gels in liquid bath

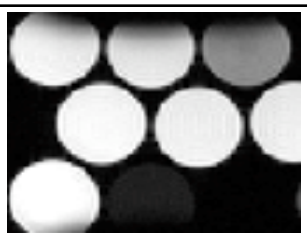

Figure 2. Example GESE images (TE=54ms), left-right increasing iron concentrations. Top row ferritin gels, middle row ferritin solutions, bottom row "iron standard" solutions

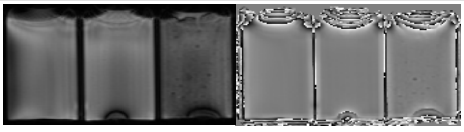

Figure 3. SWI acquired images (left) and calculated phase maps (right) of ferritin gels

Imaging: GESE [8], SWI [3] and MFC [4] sequences were run on our Signa HDx 3T MRI (General Electric, Milwaukee, WI) scanner using published parameters where possible.
Processing: GESE image reconstruction was performed offline. Corrected phase maps were calculated from the SWI as the difference between the image phase and a smoothed version of the image phase [9]. MFC images were registered and repeat volumes averaged prior to fitting for MFC coefficient [4].

## Results

Susceptibility artefacts in the MFC images at container edges were mitigated by surrounding the jars with liquid, see Fig. 1 a) vs b). The effect of increasing iron concentration (0, 100 and 200 μg/g) in the gel is evident (left-right in Fig. 1 b) and Fig. 2 top row). Similar concentrations of ferritin in saline solution, shown in Fig. 2 (middle row) do not have the same affect, with the three concentrations having iso-intense signals. The iron standards show a pronounced signal reduction with increasing concentration of iron; signal from the 200μg/g container (bottom right (Fig.2) is approximately equal to image noise. Derived MFC maps (not shown) have large variation in calculated MFC values within the containers, reducing the area in which a uniform ROI can be drawn. On the acquired SWI images (Fig. 3) the effect of increasing ferritin concentration in the gels is also clearly visualised, with what may be ferritin clumps or small air spaces seen in the 200μg/g container (far right). Some of these details are seen in the derived quantitative phase difference maps, but they mainly show gross phase changes at the container edges.

## Discussion and Conclusion

Distortions at phantom borders due to macroscopic differences in magnetic susceptibility are greatest on the MFC images, which use an EPI readout. Using a liquid bath and acquiring data with the phase-encode direction along the longest dimension of the phantom (here axially) improved distortion artefacts. Poor fitting of the MFC signal, possibly due to residual and variable distortions in the asymmetric spin echo data, further reduced the area for ROI analysis on MFC maps. Implementation of MFC using fast-spin echo sequences, or increasing the bandwidth may improve these artefacts. The iso-intensity of the ferritin solutions on acquired images for all three techniques may be due to the large ferritin molecules (~450kDa) having settled to bottom of the container, or the longer $T_2$ of the saline fluid (relative to the gel) masking the $T_2$ shortening effect of the ferritin. The decreasing signal intensity with increasing concentration in the "iron standards" suggests that the iron compounds are small enough to remain suspended within the solution. To be sensitive to the differences in magnetic susceptibility between the different iron concentrations, a more suitable phantom for SWI may be layers of gels of different concentrations within the same container. The fast setting nature of the thrombin fibrinogen-gel lends itself to this type of phantom and is to be attempted in future work.
This pilot work was carried out to investigate the MRI characteristics of three different substances suitable for use as LA-ICP-MS metal mapping matrices, and to inform the production of intermediary iron concentrations. These initial results show that the ferritin gels are the most suitable substance for the phantom.

**References**: 1. Haacke, EM, et al. Magn Reson Imaging 23 (2005) 2. Gelman, N, et al. Radiology 210 (1999) 3. Haacke, EM, et al. AJNR Am J Neuroradiol 30 (2009) 4. Jensen, JH, et al. Magn Reson Med 61 (2009) 5. Becker, JS, et al. Anal Chem 77 (2005) 6. Hallgren, B, et al. J Neurochem 3 (1958). 7. Marshall, D, LGC Tech. note (2009) 8. Cox, E, et al. Proc. ISMRM p1411 (2008) 9. Ogg, RJ, et al. Magn Reson Imaging 17 (1999).
**Acknowledgements**: Initial work of Patrick Galler, previously at LGC.