Multi-site, multi-vendor reproducibility of R2* relaxometry on an SPIO phantom at 1.5T and 3T

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Target Audience: Researchers and clinicians interested in quantitative imaging biomarkers, relaxometry, or iron quantification.

Purpose: R2* relaxometry is a highly promising technique for liver iron quantification, due to its rapid acquisition time and the linear relationship between R2* and liver iron concentration (LIC)[1]. However, it is hampered by several confounding factors (including noise and fat effects) that may introduce protocol- and platform-dependent error[2,3]. Although algorithms that correct for these confounders have been developed, the inter-platform and inter-site reproducibility of these R2* mapping techniques have not been fully established[4]. The purpose of this work was to assess the reproducibility of R2* mapping on a phantom with varying iron concentrations by scanning it at multiple sites, on multiple MRI platforms, and at both 1.5T and 3T, while reconstructing R2* maps using a common algorithm corrected for relevant confounding factors[3].

Methods: *Phantom and imaging sites:* A phantom consisting of 5 cylindrical vials (approximate diameter=22 mm, height=53 mm) with increasing iron concentrations (0, 25, 50, 75, 100 mg/l) was constructed by adding super-paramagnetic iron oxides (SPIOs, Feridex, Bayer Inc., Wayne, NJ) to an agar (2% w/v) mixture to achieve R2* values in a relevant pathophysiologic range. The same phantom was sequentially shipped to each of the imaging sites in this study, where it was scanned and shipped to the next site. Scanner vendors included Philips, Siemens and GE (including different GE models at two of the sites; see Table 1).

Site (vendor)	1.5T scanner	3T scanner
Site 1 (Philips)	Achieva	Achieva TX
Site 2 (Siemens)	Avanto	Tim Trio
Site 3 (GE)	HDxt	MR750
Site 4 (GE)	MR450w	MR750w

Table 1: *Scanner specifications at all four sites.*

Imaging protocol: At each site, the vials were placed contiguously on each scanner, horizontal and parallel to the main magnetic field. R2* mapping acquisitions were performed at both 1.5T and 3T using each site's version of a multi-echo 3D spoiled gradient echo (SPGR) sequence, with acquisition parameters described in Table 2. Data at 1.5T were obtained in a single echo train, whereas 3T acquisitions used two interleaved echo trains to achieve shorter inter-echo spacing.

	1.5T	3T
Number of echoes	6	6
TE_{init}	1.07-1.35ms	1.19-1.48ms
ΔTE	1.74-2.09ms	0.96-1.05ms
Slice thickness	4mm	4-6mm
Pixel Bandwidth	977-1754Hz	977-1470Hz
Flip angle	5-10°	3-10°

Table 2: *Summary of acquisition parameters.*

R2 map reconstruction and analysis:* Complex echo images were sent to a central site (site 3) for reconstruction of R2*. Linear phase correction along the frequency encode direction was applied when necessary to the 3T interleaved-acquisition data, to remove residual phase inconsistencies between echoes. In anticipation of applying this technique in a general clinical setting where both iron and fat may be present in the liver, we used a previously described technique for fat-corrected complex-fitting R2* quantification[3] (same algorithm applied to data from all sites). For each R2* map, measurements were performed by placing a single ROI on each of the vials on a central slice. R2* measurements from each vial were correlated to the underlying iron concentration, and compared across sites using Bland-Altman analysis. Finally, R2* measurements at 1.5T were compared with those at 3T using linear correlation.

Results: A linear increase of R2* with iron concentration was observed at all sites and both field strengths (Figure 1), with close agreement across sites (Table 3). For each site, 3T R2* values were similar to those at 1.5T (Site 1: slope=1.04±0.03, intercept=-6±13s^{-1}; Site 2: slope=1.02±0.01, intercept=-6±13s^{-1}; Site 3: slope=1.05±0.01, intercept=-12±4s^{-1}; and Site 4: slope=1.05±0.01, intercept=-9±5s^{-1}). The correlation coefficient (r^2) was >0.996 in all cases.

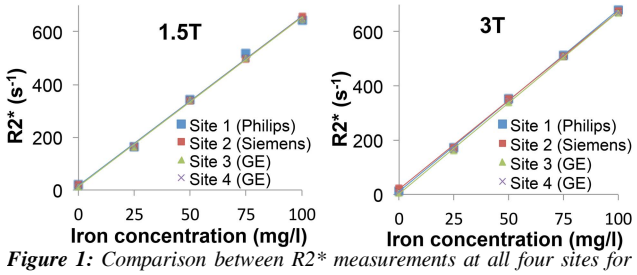

Figure 1: *Comparison between R2* measurements at all four sites for each of the field strengths: (left) 1.5T, (right) 3T. A linear increase of R2* with iron concentration was observed (r^2>0.996 in all cases), with good agreement between sites at each field strength (Table 3).*

Discussion: Excellent R2* measurement reproducibility was observed in phantoms across different sites and platforms. The limits of agreement between different sites (Table 3) are similar to the repeatability limits of agreement for in vivo R2* measurement in liver, (-17,16) s^{-1} as recently determined by Hines et al in patients without iron overload[5]. These phantom results suggest that R2* relaxometry may enable reproducible iron quantification at different sites.

The source of iron used in this study does not fully reproduce the MR effects of liver iron: the magnetization of ferumoxides (Feridex) is nearly saturated at 1.5T[6], unlike ferritin and hemosiderin in the liver. Hence, phantom R2* is similar at 1.5T and 3T, whereas liver R2* increases linearly with field strength in patients with liver iron overload. However, this difference should not play a major role in this study, aside from limiting the range of R2* observed at 3T.

	1.5T		3T	
	Mean difference	95% agreement	Mean difference	95% agreement
Site 1 vs Site 4	4.6 s^{-1}	(-12,21) s^{-1}	6.0 s^{-1}	(2,10) s^{-1}
Site 2 vs Site 4	1.2 s^{-1}	(-4,6) s^{-1}	6.9 s^{-1}	(-3,17) s^{-1}
Site 3 vs Site 4	1.9 s^{-1}	(-11,15) s^{-1}	-2.3 s^{-1}	(-9,4) s^{-1}

Table 3: *Summary of Bland-Altman comparisons between sites.*

In this study, reproducibility was observed across different scanner models from different manufactures at each field-strength, despite differences in the SPGR protocols. Different protocols affect the signal-to-noise ratio (SNR) of the acquired signal. Protocols with higher SNR (eg: using shorter echoes) are expected to achieve accurate R2* measurement over a wider range of LICs. However, this limit was not reached in the present study.

Conclusion: R2* mapping in SPIO phantoms can be performed with excellent reproducibility across sites and platforms, over a wide range of R2* values. Multi-center in vivo studies with iron overload patients are needed to extend these results for clinical R2*-based liver iron quantification.

References: [1]Wood, Blood 2005:106:1460-1465. [2]Sirlin, MRICNA 2010;18:359-381. [3]Hernando, MRM; 2013:70:1319-1331. [4]Kirk, JMRI 2010; 32:315-319. [5]Hines, JMRI 2011;33:873-881. [6]Jung MRI; 1995;13:661-674.

Acknowledgements: The authors acknowledge the support of the NIH (R01 DK083380, R01 DK088925), and the WARF Accelerator Program. We also thank GE Healthcare, Philips and Siemens for their support.