### Non-linear relationship between estimated liver iron concentration and R2\*

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#### TARGET AUDIENCE

Users of clinical MR liver iron measurements as well as those who seek to develop and optimize those measurements. Researchers with an interest in  $R_2^*$  and the mechanisms that generate  $R_2^*$ .

### INTRODUCTION

There are several MRI methods to assess liver iron concentration (LIC). In our hospital we use a standardized protocol combining a number of these approaches, including  $R_2^*$  measurement, and LIC-assessment following Gandon's method [1]. The analysis of patient LIC-assessments with these two methods, from Jan 2008 until Dec 2013, is presented here.

# **METHODS**

All patients were scanned with the same protocol on a Siemens Avanto 1.5T. In case of multiple measurements for a patient, only the first one was included. In this way we obtained 95 individual measurements in a six year's period.  $R_2^*$  was measured with a spoiled gradient echo sequence (SpGE), TR = 300 ms,  $\alpha = 20^\circ$ , 12 echoes TE = 100 ms

$$S_T(TE) = S_{T0} \cdot e^{-R_2^* \cdot TE} \tag{1}$$

$$S(TE) = \sqrt{S_T^2(TE) + v^2}$$
 (2)

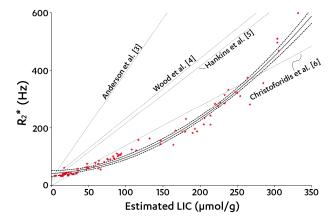
0.99 cdots 16.5 ms, using a surface coil. For Gandon's method we acquired five SpGE sequences with TRs and TEs according to [1], using the body coil for signal acquisition. Since the signal of SpGE-sequences is heavily influenced by  $B_0$ -inhomogeneities across the slice, we aimed at optimal shimming by measuring no more than three transversal 10 mm slices in one breathhold, applying a manually defined shim region fitting the body tightly, excluding arms and air. ROIs of the liver were manually drawn, excluding visible blood vessels. To calculate  $R_2^*$  the ROI-averaged signals were fitted to the combination of eqs. 1 and 2. Eq. 1 describes the true signal, depending on the parameters  $S_{T0}$  and  $R_2^*$ . Eq. 2 describes an approximated Rician noise bias with the parameter v. Gandon's analysis was performed with the same liver ROI as for  $R_2^*$ , compared to a ROI of the paraspinal muscles. The algorithm was taken from Gandon's web-site [2].

### RESULTS

The figure shows the  $R_2^*$  values against the LIC values for all measurements (red stars). There is a clear non-linear relationship, which was approximated (fitted) with a quadratic function: eq. 3 (solid line, with dashed lines as 95% CI). For comparison, a number of (linear) relationships found in literature are shown (dotted lines).

## **DISCUSSION**

The clear non-linear relationship we find is remarkable. The data from Christoforidis et al. [6] lie in the same range as our data, but their error variations are larger, rendering it difficult to distinguish a possible non-linearity. Since our experience learns that a factor of 2 overestimation of  $R_2^*$  due to bad shimming is not exceptional, we are tempted to attribute the fact that the authors [3-5] report much larger values of  $R_2^*$  to suboptimal shimming. A limitation



$$R_2^* = 41.7 + 0.149 \cdot LIC + 4.04 \cdot 10^{-3} \cdot LIC^2$$
 (3)

of our data might be the absence of biopsy confirmation. Biopsy, however, has been replaced by MRI methods that are now standard care for determining LIC. A consecutive series with biopsy confirmation therefore is not feasible. A theoretical exploration of the non-linear behaviour of  $R_2^*$  would be of interest, but this is outside the scope of this abstract.

### CONCLUSION

Accurate measurements with careful shimming reveal a non-linear relationship between  $R_2^*$  and LIC.

REFERENCES [1] Gandon Y, Olivie D, Guyader D et al. Lancet (2004) 363:357-362. [2] http://www.radio.univ-rennes1.fr/Sources/EN/Hemo.html [3] Anderson LJ, Holden S, Davis B et al. Eur Heart J (2001) 22:2171-2179. [4] Wood JC, Enriquez C, Ghugre N et al. Blood (2005) 106:1460-1465. [5] Hankins JS, McCarville MB, Loeffler RB et al. Blood (2009) 113:4853-4855. [6] Christoforidis A, Perifanis V, Spanos G et al. Eur J Haematol (2009) 82:388-392