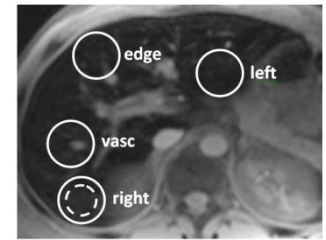


# ASSESSMENT OF IRON OVERLOAD IN THE LIVER WITH MRI T2\*. THE EFFECTS OF THE ANALYSIS TECHNIQUE ON T2\* ESTIMATION

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**INTRODUCTION:** MRI T2\* imaging has been widely used for evaluating iron overload [1]. A linear relationship has been shown between R2\* (the inverse of T2\*) and iron content over the entire clinical range of interest [2]. Although the process of calculating T2\* is conceptually straightforward, there are a number of factors related to image analysis that could affect the measured T2\*, including the signal averaging method, location of the selected region-of-interest (ROI) and whether it includes vasculature, selected exponential fitting model, and number and values of echo times (TE's) at which data is acquired [2-4]. In this study, we investigate the influence of these factors on estimating T2\*.

**METHODS:** Calibrated phantoms with iron concentrations from 25 to 225 µmol/g were created to compare the measured T2\* values to ground truth. The phantoms were imaged on a 3.0T Siemens MRI scanner using a 12-echo GRE sequence with TE =1-16.5 ms. Eleven human subjects with different degrees of iron overload were imaged on a 3.0T Siemens scanner, where a mid-liver axial slice was acquired in a single end-expiration breath-hold. The images were analyzed using the T2\* mapping software on the scanner console that is used for clinical use, where a circular ROI of about 4 cm<sup>2</sup> was selected inside the phantoms' cross-sections and in the liver's right lobe away from vasculature. Software was created in Matlab to analyze the images while modifying different factors (Fig. 1), including the signal



**Figure 1.** Locations and sizes of different ROIs used for calculating T2\*.

averaging method; exponential fitting model (using the Levenberg–Marquadt algorithm); ROI size (4 cm<sup>2</sup> and 2 cm<sup>2</sup>); ROI location (in the right and left lobe); vascular inclusion; edge effect; data truncation (removing late echoes based on visual assessment); and the effect of the degree of iron overload on the results (a cutoff T2\* of about 10 ms was used to differentiate between normal and iron-overloaded tissues, in accordance with literature [5]). Inter- and intra-observer variabilities were studied for measuring T2\*. The signal averaging methods included: pixel-wise (PIXEL), where exponential fitting is applied to each pixel inside the ROI, followed by obtaining the mean of the resulting T2\* values; average (AVG), where average signal intensity inside the ROI is first calculated, followed by exponential fitting of the resulting values at different TE's; and median (MED), where median signal intensity inside the ROI is first calculated, followed by exponential fitting of the resulting values at different TE's. The exponential fitting models included: single-exponential (SNGL-EXP) model:  $S = S_0 \times \exp^{-TE/T2^*}$ , bi-exponential (BI-EXP) model:  $S = 0.9S_0 \times \exp^{-TE/T2^*} + 0.1S_0 \times \exp^{-TE/200}$  and exponential-plus-constant (CNST-EXP) model:  $S = S_0 \times \exp^{-TE/T2^*} + C$ .

**RESULTS:** In the phantom experiments, T2\* ranged from 19.5 to 2.3 ms for iron concentration from 25 to 225 µmol/g, respectively. The R2\* values, measured on the scanner software, showed excellent linear relationship with iron concentration. When the T2\* values calculated using different analysis techniques were compared to those measured on the scanner console, the SNGL-EXP model combined with PIXEL method (SNGL-EXP + PIXEL) and the BI-EXP model combined with AVG method (BI-EXP + AVG) provided the best agreements, followed by CNST-EXP + AVG, BI-EXP + MED, and CNST-EXP + MED. The remaining techniques resulted in incorrect T2\*, especially for small iron contents.

In the liver experiments, T2\* ranged from 4.2 to 16.2 ms. As shown in Table 1, the SNGL-EXP model and PIXEL method resulted in close agreement with the values obtained on the scanner console, which was maintained in both normal and iron overloaded groups, with the latter group showing better agreement. The results showed differences in T2\* measurement based on the ROI size and location. The AVG and MED methods showed similar performances in terms of measurement error and regression analysis. Both the AVG and MED methods showed less sensitivity to changes in the ROI size, location, inclusion of vasculature, and proximity to the liver boundary, than did the PIXEL method (the PIXEL method resulted in double the error produced by the AVG or MED method). The SNGL-EXP model was less affected by changes in the selected ROI (measurement error reduced by 50%) than was the CNST-EXP or BI-EXP model. Inter- and intra-observer analysis showed low variabilities: largest agreement with the AVG, followed by MED, and then the PIXEL methods. Truncating the largest echoes did not affect T2\* estimation (P = 0.473).

**CONCLUSIONS:** MRI T2\* measurement is a promising technique for evaluating hepatic iron overload. However, various factors associated with image analysis could affect the resulting measurements. The user should be aware of the effects of these factors, such that the resulting T2\* values are interpreted with caution, especially when they are compared to other values calculated using different analysis techniques. The encouraging results in this study require conducting further research on a larger number of patients with wider ranges of iron overload and known pathology to confirm the results and determine the optimal technique for evaluating iron overload in different diseases and patient groups.

**REFERENCES:** [1] Br J Radiol; 67:339-341 ; [2] Magn Reson Imag; 27:188–197; [3] J Mag Reson Imag; 33:348–355; [4] Eur J Haematol; 76:183-192; [5] Hemoglobin; 36: 343-361.

ROI Method	PIXEL	AVG	MED
cc /avg abs err	0.915 / 2.65	0.380 / 4.79	0.365 / 4.86
Regression	y = 1.24x+0.24	y = 0.33x+2.03	y = 0.36x+1.96
<b>Iron content</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
norm(5):cc/err	0.570 / 3.73	-0.330 / 6.56	-0.330 / 6.72
overload (6)	0.89 / 1.75	0.84 / 3.32	0.81 / 3.3
<b>Exp. Model</b>	<b>SNGL-EXP</b>	<b>BI-EXP</b>	<b>CNST-EXP</b>
cc /avg abs err	0.915 / 2.65	0.955 / 15.30	0.951 / 16.56
Regression	y = 1.24x+0.24	y = 3.72x+10.94	y = 3.95x-1.83
<b>Iron content</b>	<b>SNGL-EXP</b>	<b>BI-EXP</b>	<b>CNST-EXP</b>
norm(5):cc/err	0.570 / 3.73	0.690 / 25.02	0.670 / 27.07
overload (6)	0.89 / 1.75	0.98 / 7.21	0.98 / 7.82
<b>ROI Size</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.927 / 1.03	0.995 / 0.42	0.992 / 0.52
Regression	y = 0.67x+2.50	y = 1.41x-1.59	y = 1.48x-1.87
<b>Vasculature</b>	<b>SNGL-EXP</b>	<b>BI-EXP</b>	<b>CNST-EXP</b>
cc /avg abs err	0.889 / 2.93	0.882 / 5.71	0.882 / 6.23
Regression	y = 1.07x+2.32	y = 1.12x+2.48	y = 1.13x+2.53
<b>Vasculature</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.889 / 2.93	0.889 / 1.05	0.916 / 1.24
Regression	y = 1.07x+2.32	y = 0.29x+2.92	y = 0.26x+3.01
<b>Edge</b>	<b>SNGL-EXP</b>	<b>BI-EXP</b>	<b>CNST-EXP</b>
cc /avg abs err	0.616 / 3.31	0.596 / 7.76	0.575 / 8.58
Regression	y = 0.88x+3.02	y = 0.60x+6.2	y = 0.59x+7.03
<b>Edge</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.616 / 3.31	0.995 / 0.74	0.980 / 0.75
Regression	y = 0.88x+3.02	y = 0.62x+1.37	y = 0.72x+0.86
<b>Location</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.580 / 5.85	0.970 / 1.95	0.975 / 1.69
Regression	y = 0.98x+6.15	y = 4.73x-14.12	y = 3.90x-11.00
<b>Inter-observ.</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.990 / 0.47	0.996 / 0.37	0.985 / 0.46
Regression	y = 0.96x+0.33	y = 0.82x+0.57	y = 0.83x+0.48
<b>Intra-observ.</b>	<b>PIXEL</b>	<b>AVG</b>	<b>MED</b>
cc /avg abs err	0.952 / 0.67	0.998 / 0.22	0.989 / 0.35
Regression	y = 0.86x+1.11	y = 0.84x+0.66	y = 0.75x+1.07
<b>Echo Trunc.</b>	<b>SNGL-EXP</b>		
cc /avg abs err	0.932 / 1.55		
Regression	y = 1.29x-1.25		

**Table 1. Patient results.** Correlation coefficient (cc), measurement error, and regression equation for calculating T2\* in patients using different analysis techniques. The ROI method was fixed to PIXEL when comparing different models. The model was fixed to SNGL-EXP when comparing different ROI selection methods. Large ROI was used for all analyses, except in the ROI Size row. The ROI in the liver's right lobe was used in first 5 rows. The model and method were fixed to SNGL-EXP and PIXEL in the last 6 rows.