# MRI- R2* Relaxometry for assessment of kidney iron accumulation as a cause of renal dysfunction in patients with sickle cell disease (SCD)

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**Target Audience**

Clinicians and scientists dealing with the treatment of rare diseases needing chronic blood transfusions and following excessive body iron accumulation. Especially diseases like hereditary hemochromatosis (HHC), sickle cell disease (SCD), and transfusion-dependent thalassemia (TDT) MRI can help to measure the iron content in diverse organs by R2* relaxometry.

**Introduction/Purpose**

In recent years, hepatic and cardiac iron deposition has been studied in detail. Due to its involvement in the development of renal dysfunction –a frequent co-morbidity in iron overload diseases (Powers DR et. al. 2005) – renal iron should become a field of interest. This study aims to determine the renal iron disposition in patients with iron overload, especially in patients with sickle cell disease (SCD), and transfusion dependent thalassemia (TDT).

**Material and Methods**

Patients with transfusion-dependent thalassemia (TDT: n=10, age mean 28 ± 11y), hereditary hemochromatosis (HHC: n=5, age mean 51±11y), sickle cell disease (SCD: n=10, age mean 26±13y), and healthy controls were studied at our units for clinical liver iron (LIC by biomagnetic liver susceptometry, SQUID-BLS), relative cardiac and renal iron assessment (by MRI-R2*/T2*). Serum lactate dehydrogenase (LDH) levels were also determined.

For assessment of the transversal relaxation rate R2* scans were performed using a breath hold prospective ECG gated (GRE) sequence [12 bipolar echoes, echo time (TE) = 1.3-25.7ms, Δt= n·1.16ms, pulse repetition time (TR) = 244ms, flip angle = 20°, bandwidth 1955 Hz/pixel] on a 1.5 T MRI (Siemens AG, Erlangen). A mid-vertebral slice (thickness = 10 mm, pixel resolution 1.25x1.25 $mm^2$) was selected covering the major part of the liver, spleen, bone marrow, and kidneys. For the kidneys, a stack of 4-8 of slices without gaps (thickness=5.5mm, pixel resolution 1.25x1.25$mm^2$). The in vivo liver iron concentration (LIC: dry-weight conversion factor = 6) was measured by biomagnetic liver susceptometry (SQUID-BLS).

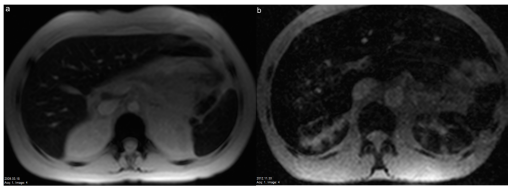

**Fig. 1:** Iron assessment by MRI-R2* in the left renal cortex of patients with hemolytic anemia and matched LIC (images at TE=4.6 ms). **Left**: Patient with ß-thalassemia major (30 y): R2* = 35 $s^{-1}$, LDH = 100 U/L, LIC = 2665 ± 300 µg/$g_{liver}$; **Right**: Patient with sickle cell disease (34 y): R2* = 475 $s^{-1}$, LDH = 987 U/L, LIC = 2814 ± 174 µg/$g_{liver}$.

Signal intensity data from the cortex of the left and right kidney were assessed by CMRtools (Cardiovascular Imaging Solutions Ltd). Renal signal intensities, averaged over different ROIs positioned on the cortex and medulla, and were fitted (Levenberg-Marquardt algorithm) to the well known mono-exponential model with constant signal level offset (equation 1).

$$(1)\quad |S(t)| = S_w(0)\cdot\exp(-R2_w^*t) + S_{LO}$$

*Statistical analysis:*

Linear correlation analysis was performed by parametric statistics (Pearson) in order to estimate the association between the cortical renal iron accumulation and liver iron as well as hematological blood parameters, especial the LDH. As, consistent with prior anatomic and imaging studies (Lande IM. et. al. 1986), iron concentration was predominantly found in the renal cortex, we used the cortical iron concentration for statistical analysis.

**Results**

Cortical renal R2* (mean ± SD) was significantly higher in Patients with SCD (141±132 $s^{-1}$) than TDT (29±20 $s^{-1}$) and HHC (15±2 $s^{-1}$), ($p<0.05$) see Fig. 1 and 2. As found in former studies (Schein et. al.) no significant correlation was observed between renal R2* and LIC (2655±1924µg/$g_{liver}$), (p=0.26) see Fig. 3. Significant correlation was found between renal R2* and serum LDH ($r^2=0.8$, $p < 0.001$), whereas serum bilirubin did not correlate (p= 0.86).

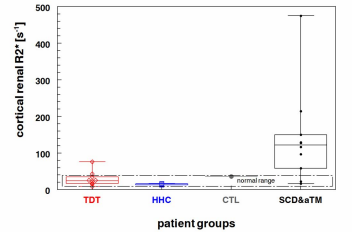


**Fig. 2:** Boxplot analysis of cortical renal R2* in TDT (R2*=29±20 $s^{-1}$), HHC (R2*= 15±2 $s^{-1}$), SCD (R2*= 141±132 $s^{-1}$) and controls (R2* = 36 $s^{-1}$).Error bars represent SD.

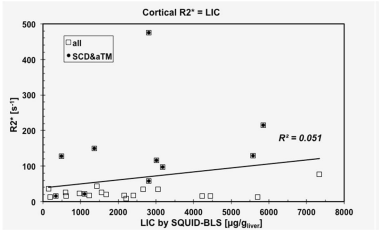


**Fig. 3:** Kidney R2* (141±132 $s^{-1}$) as a function of LIC (2655±1924µg/$g_{liver}$) determined by SQUID-BLS. Kidney R2* did not correlate with LIC ($r^2=0.22$, p=0.26).

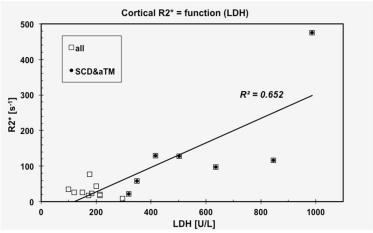


**Fig. 4:** Kidney R2* (141±132 $s^{-1}$) as a function of serum LDH (579 ± 256 U/l). There was a highly significant correlation observed (($r^2=0.8$, $p<0.001$).

**Discussion/Conclusion**

It still remains a matter of debate whether iron accumulation in kidney is caused by blood transfusion therapy or intravascular hemolysis. As patients suffering sickle cell disease accumulate significantly higher iron in the kidney, independently of the total iron burden represented by LIC, it seems to be likely that intravascular hemolysis is the underlying cause of renal involvement. As assumed by previous studies, kidney iron accumulation decreases during blood transfusion therapy and somatic growth. Further studies will be conducted to compare the effect of transfusion therapy on kidney iron burden in patients with SCD.

**References**

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**Key words**

T2*, R2*, Iron, Relaxometry, MRI- R2*, SQUID_BLS, Liver, Kidney, SCD, TDT