

Pancreatic Iron Load measured with MRI R2*: Distribution within the Organ in Comparison with Cardiac and Hepatic Iron

Jin Yamamura¹, Björn P Schönengel¹, Moritz Brehmer¹, Christoph Berliner¹, Sarah Keller¹, Charlotte Pfeifer², Gerhard Adam¹, and Roland Fischer^{3,4}

¹Diagnostic and Interventional Radiology, University Medical Center-Hamburg, Hamburg, Hamburg, Germany, ²Center of Oral & Dental Surgery - Department of Radiology, University Medical Center-Hamburg, Hamburg, Hamburg, Germany, ³Pediatric Hematology, University Medical Center-Hamburg, Hamburg, Hamburg, Germany, ⁴Children's Hospital and Research Center Oakland, Oakland, CA, United States

Introduction/Purpose

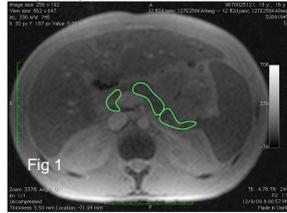
Chronically transfused patients as well as patients with hereditary hemochromatosis (HHC) are affected by complications due to the excessive body iron accumulation (Gordeuk et al 1987). In recent years assessment of the body iron storages using non-invasive magnetic resonance tomography (MRI) using R2- (T2) or R2* (T2*) relaxometry has become more and more a standard and convenient method. The comparison and correlation of the iron storages in different organs or tissues in order to detect specific interorganic relationships or iron loading patterns has been subject of many thalassemia and iron loading studies. The study aims to thoroughly determine the cardiac, hepatic and pancreatic iron deposition with focus on the iron storages in the three pancreas regions, i.e. head, body and tail in a cohort of chronically transfused patients with or without β -thalassemia major and patients affected with hemochromatosis. The results were correlated to each other.

Material and Methods

68 patients affected with β -Thalassemia major (TM: n = 41; 15 splenectomized), hereditary hemochromatosis (HHC: n = 11), transfusion dependent iron overload (BTX: n = 9) or Diamond-Blackfan anemia (DBA: n = 7; 1 splenectomized) were scanned for cardiac, hepatic, and pancreatic iron by R2*. All DBA patients (7/7) as well as the majority of the TM patients (39/41) and the patients with transfusion dependent iron overload (8/10) chronically received blood transfusions. HHC patients were not treated by phlebotomy therapy. A group of 10 healthy subjects served as controls.

For heart iron measurements, a mid-papillary short axis slice (10 mm) was selected. A mid-vertebral slice (thickness = 10 mm, pixel resolution 1.25x1.25 mm²) was selected covering the major part of the liver, spleen, and bone marrow. For the pancreas, a stack of 4-8 of slices without gaps (thickness = 5.5 mm, pixel resolution 1.25x1.25 mm²). All MRI-scans were performed as breathhold prospective ECG gated MRI sequences with data from typically 9 heartbeats in end-diastole on a 1.5 T imager (Siemens) with 12 bipolar echo times TE= 1.3 to 25.7 ms (Δt = n-1.16 ms, TR = 244 ms, flip angle = 20°, band width 1955 Hz/pixel).

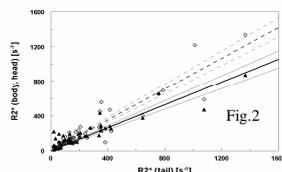
Signal intensity data were assessed by CMRtools (Cardiovascular Imaging Solutions Ltd). Cardiac and liver ROI based R2* were determined in the interventricular septum of a mid-papillary short axis slice and in a mid-vertebral slice covering the whole liver. Pancreas signal intensities were averaged from three different ROIs positioned on the tail, body and head of the pancreas (Fig. 1).



A water/fat separation technique to the in-phase and out-of-phase signal intensities as described by Wehrli et al (1991)

Results

R2* of pancreatic tail, body and head were well correlated as tested by the spearman rank correlation coefficient rs (tail vs. body: rs=0.92, p<10⁻⁴; tail vs. head: rs=0.81, p<10⁻⁴) (Fig 2). Cardiac and pancreatic R2* values did significantly correlate with each other (spearman rank correlation coefficient rs=0.57, p<0.0001) (Fig 3). From 39 patients exceeding the high risk threshold for cardiac iron of pancreatic R2*>100 s⁻¹, 58.9% (23/39) also had a septal cardiac R2*>40s⁻¹, while 58.6 % (17/29 TM) of patients with TM only exceeded these thresholds. A high significant correlation between the R2* values of the liver and the pancreas could be revealed. Including all patients the spearman rank correlation coefficient rs was 0.37 (p=0.003) while the correlation between the pancreatic R2* and the hepatic R2* for patients only affected with TM was quite better (rs=0.56; p=0.0002).



Conclusion

R2* measurements can be adequately used for determining the iron concentration within the pancreas, although the water/fat separation technique should be applied. There seems to be a complex coherence in the iron burden within different organs. Patients with iron overload in pancreas and other organs can be justly detected by MRI-R2* and treated right before organic failure. **Key words:** T2*, R2*, Iron, Relaxometry, Fat-Water, Chemical shift

was applied. This approach results in different relaxation rates R2w* and R2f* for water and fat in equation 1:

$$(1) |S(t)| = Sw(0) \cdot \exp(-R2w^*t) \sqrt{1 + (Sf(0)/Sw(0))^2 \cdot \exp[2(R2w^*-R2f^*)t]} + 2(Sf(0)/Sw(0)) \cdot \exp[(R2w^*-R2f^*)t] \cdot \cos(\square t)$$

In the presence of local field distortions by iron the relaxation rates are affected in a similar manner by R2w* = R2f*. Taking also a signal level offset (SLO, noise) into account, equation 1 can be reduced to the final fit function 2, especially if $\square = \text{const} = 0.217 \text{ kHz}$:

$$(2) |S(t)| = Sw(0) \cdot \exp(-R2w^*t) \sqrt{1 + (Sf(0)/Sw(0))^2} + 2(Sf(0)/Sw(0)) \cdot \cos(\square t) + \text{SLO}$$

An apparent fat-water ratio (aFWR) can be calculated from the signal amplitudes Sw(0) and Sf(0) according to O'Regan et al (2008) and equation 3:

$$(3) \text{aFWR} = Sf(0) / [Sf(0) + Sw(0)]$$

In tissues with no fat infiltration (Sf(0) = 0), equation (2) will become the well known mono-exponential model with constant signal level offset (equation 4). This 3-parameter model was fitted to the signal intensities of heart and liver in most patients.

$$(4) |S(t)| = Sw(0) \cdot \exp(-R2w^*t) + \text{SLO}$$

Levenberg-Marquardt algorithm was used to fit the beat frequency pattern.

Statistical analysis:

Linear regression was performed to estimate the relationship between the iron loading in the three different pancreas regions. The relationship between cardiac and pancreatic iron loading as well as hepatic and pancreatic iron loading was estimated by Spearman correlation.

ROC analysis was performed between cardiac and pancreatic R2* to determine how well pancreatic iron served as a surrogate for cardiac iron deposition.

