MRI based Noninvasively Differentiation between Aggregated and Dispersed Liver Iron in vivo: a feasibility study

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Target Audience. Scientists involved in liver iron content (LIC) research who like to address different aspects of liver iron overload.

Purpose. To test an MRI method published previously which has the potential to discriminate between aggregated and dispersed iron.

Theory. Jensen et al. [1] give the following equation for signal intensity S at time t of a multi-contrast spin-echo (MC-SE) sequence:

$$S(t) = S_0\, e^{-RR2\, t}\, \exp(-A^{3/4}\, \Delta t^{3/4}\, t^{3/8}) \tag{1}$$

with S_0: signal at t = 0, RR2: reduced transverse relaxation rate, A: aggregation index, and Δt: half the echo-spacing. Equation (1) is valid only at time points where spin-echoes occur, i.e. t = 2N Δt, where N indicates the echo number.

Methods. 22 patients (age 8 … 59 years, mean age 23.5 y; 13m, 9f) suspected for liver iron overload were examined by MRI to test the feasibility of addressing the nature of LIC in vivo. All examinations were performed at 1.5 T (Siemens Avanto, Iselin, NJ) using spin-echo (SE) and two different multi-contrast spin-echo (MC-SE) sequences acquired with four different Δt values of 2,3,4 and 6 ms, i.e. echo spacings of 4, 6, 8 and 12 ms. One of the MC-SE sequences had a refocusing pulse with three-fold the slice thickness of the excitation pulse [2] and is referred to as 3sr in the following, the other was a standard sequence. LIC was determined from SE data with commercial analysis by Ferriscan® taken as reference. Patients exceeding the upper limit of 769 mmol/kg for this method were excluded. MC-SE data was fitted to theory according to (1) yielding two parameters, namely reduced transverse relaxation rate (RR2) and aggregation index A. The Levenberg-Marquardt fit procedure was used and tested for reliability with simulations. Coefficients of determination from linear regression between these two parameters and LIC were determined.
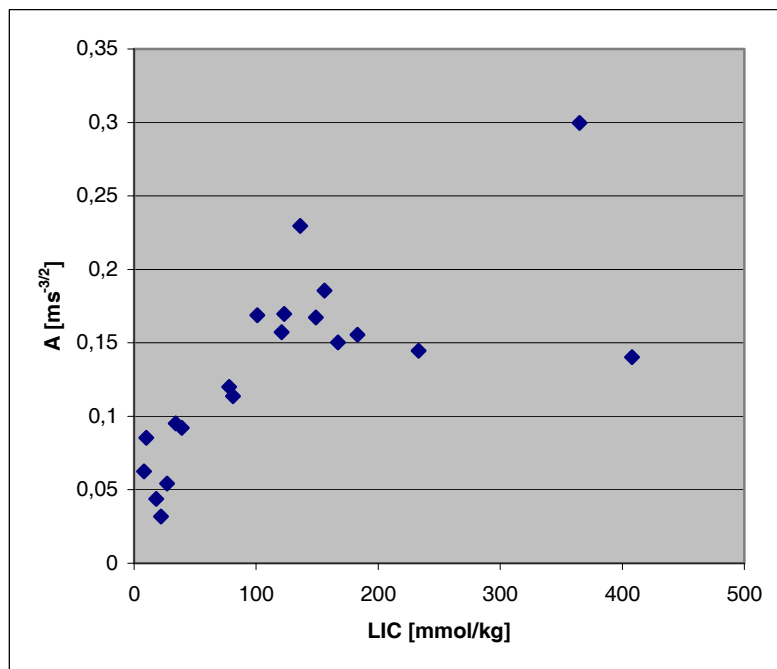

Fig. 1. Aggregation index A as a function of LIC.

Results. Two patients had to be excluded due to exceeding the LIC limit for SE analysis. Simulations showed the fit procedure to be stable and reliable with deviance of max. 10%. Only very low A values below 0.002 ms$^{-3/2}$ couldn't be separated from each other.

Fit quality was good in patient data with chi-square below 15 in most cases and less than 20 iterations.

The aggregation index A turned out to correlate with LIC (c.f. Fig. 1) when considering the data acquired with the 3sr sequence. Coefficient of determination was 0.53. RR2 values ranged from 12 to 40 s^{-1} independently of LIC (not shown). Alike, A and RR2 evaluated from data acquired with the standard MC-SE sequence did not correlate to LIC (not shown).

Discussion. Our results indicate that in vivo determination of aggregated iron seems to be feasible by the aggregation index A. Positive correlation of this parameter to LIC goes in line with iron storage mechanisms in liver which are known to be based on aggregated iron. In vitro, RR2 is proven to address dispersed iron stores [1]. In vivo, this parameter has been proven to be useful for addressing iron content of heart muscle [3]. Lack of correlation between this parameter and LIC is a hint to liver iron storage differing from heart.

It has to be stressed that correlation is detected only with a special sequence mentioned in [1] and [3] with modified slice-selective refocusing pulses, named 3sr above. The corresponding slice thickness was three-fold the excitation slice thickness in order to minimize effects of T_1w stimulated echo contributions to the signal [2]. Our results show that these interferences can not be neglected.

Conclusion. Evaluation of aggregated liver iron fraction is feasible. Compared to the results published in [3], our results indicate that iron storage mechanisms in the liver may differ from those in heart muscle.

References.
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