Gedruckter Konferenzbetrag: „Biomag 2002“ in Jena

# Biomagnetic liver susceptometry in children with transfusional iron overload, younger than 4 years

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## Abstract

Patients with transfusional dependent anemias are at risk for severe iron overload from blood transfusion. Starting iron chelation treatment in children as early as possible helps to avoid this risk from iron toxicity. In order to minimize also the risk from chelation toxicity, it is necessary to adjust the chelation treatment to the actual iron status assessed by the liver iron concentration.
In 1989 - 2002, SQUID biosusceptometry has been used in our department to assess iron stores in more than 2000 patients suspected for iron overload. Especially in children, biomagnetic non-invasive liver susceptometry (BLS) is the method of choice [1].

## 1 Patients and Methods

The liver iron concentration (LIC) was measured non-invasively with the Hamburg Biosusceptometer in 23 very young patients (see **Tab 1**), before the onset of iron chelation treatment. The mean age of the children was 3 years (range 1.7y – 4.0 y). These patients were diagnosed for: ß-thalassemia major (n=9), α-thalassemia major (n=4), Diamond-Blackfan anemia (n=3), sickle-cell disease SCD (n=3), leukemia (n=2), congenital dysplastic anemia CDA (n=1), rare anemia (n=1).

Biomagnetic liver susceptometry was performed by lowering the patient in the known localized magnetic dc-field ($B_{max}$= 20 mT, gradiometer 1$^{st}$ order) of the Hamburg Biosusceptometer (BTi) with water as the reference medium. The fluxintegral contributions for the liver and torso were calculated in advance for certain distances and radii (3 - 25 cm) as ellipsoids (liver) and as hemispheres or cylinders (torso). The calculated fluxintegrals were fitted over distances and radii and the coefficients were tabulated and stored in the computer for the analysis of the measurements.
In BLS, the magnetic flux change (rf-SQUID voltage output) detected by two 2$^{nd}$order gradiometer pickup coils was fitted by the superficial thorax tissue (ribs, muscle, fat; near field) and the liver tissue (far field) flux integral contributions in a 2-layer model [2]. For the biosusceptometric measurement, the patient had to be positioned by sonographic imaging for the best liver position.
During the measurement procedure of about 10 minutes, the patient should stop moving. 4 children had to bee sedated with 10mg/kg $_{\text{body weight}}$ chloralhydrate pr (patients no. 2, 4, 11 and 12; 1.7 – 2.5 y), because they did not tolerate the measurement procedure at all.

Laboratory tests (serum ferritin) and other data were obtained from clinical records

Tab 1 Listing of patients with age < 4 years at first biomagnetic liver susceptometry (BLS, see text for diagnosis).

| Patient no. | Age [years] | BLS [µgFe/$g_{ww}$] | Diagnosis |
|---|---|---|---|
| 1 | 3,2 | 4210 | ß-Thal_major |
| 2 | 1,7 | 3680 | ß-Thal_major |
| 3 | 3,7 | 5011 | ß-Thal_major |
| 5 | 2,5 | 1877 | ß-Thal_major |
| 5 | 3,3 | 2473 | ß-Thal_major |
| 6 | 2,9 | 3456 | Diamond-blackfan |
| 7 | 3,2 | 4524 | Diamond-blackfan |
| 8 | 3,5 | 3684 | Congenital dysplastic anemia |
| 9 | 2,9 | 3579 | Diamond-blackfan |
| 10 | 3,0 | 4400 | a-Thal_major |
| 11 | 2,5 | 3208 | a-Thal_major |
| 12 | 2,2 | 1660 | a-Thal_major |
| 13 | 3,4 | 867 | a-Thal_major |
| 14 | 1,8 | 2003 | a-Thal_major |
| 15 | 3,9 | 2468 | a-Thal_major |
| 16 | 3,0 | 3479 | a-Thal_major |
| 17 | 3,0 | 217 | Sickle-cell disease |
| 18 | 4,0 | 3528 | ß-Thal_major |
| 19 | 3,0 | 345 | Sickle-cell disease |
| 20 | 1,8 | 196 | Sickle-cell disease |
| 21 | 3,3 | 469 | Rare anemia |
| 22 | 3,2 | 1402 | Leukemia |
| 23 | 3,5 | 964 | Leukemia |

# 2 Results

The liver iron concentration at first BLS measured in every child is listed in Tab 1. The median serum ferritin level at this time was 1704 µg/l (range 209 – 3630, normal: 35 - 235).
The median LIC was 2468µgFe/$g_{liver}$ (range 196 – 5011). In normal children the range is 80 to 370µgFe/$g_{liver}$ [3]. Liver iron concentrations above the threshold for an increased risk of iron induced complications in thalassemic patients (i.e., > 2100 µgFe/$g_{liver}$ [4] ) was found in 12 patients. In 4 patients we found LIC values between 196 and 469µgFe/$g_{liver}$ (3 sickle-cell disease, 1 rare anemia).
In 6 patients, three or four liver iron concentration measurements could be performed in a time interval between 0 and 1450 days (**Fig 1**).

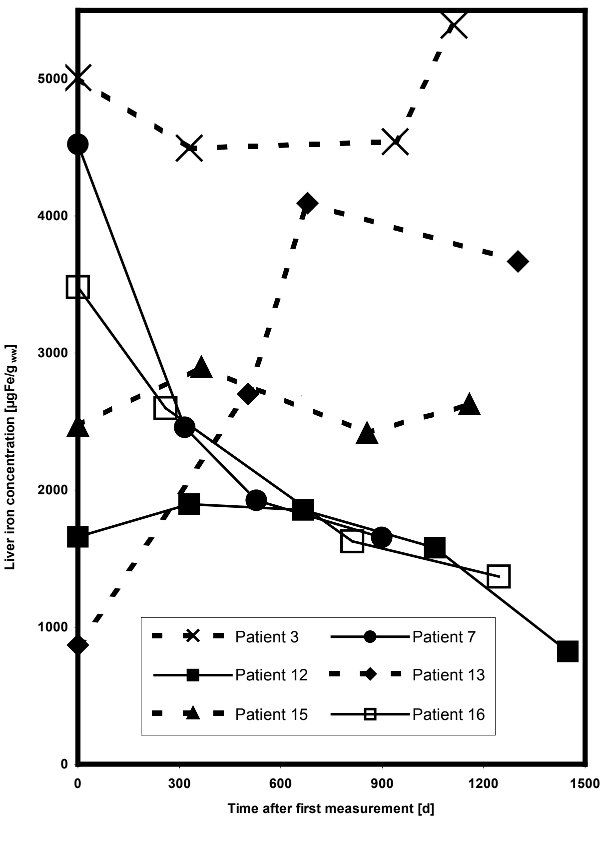


**Fig 1** Liver iron concentrations from 6 patients in the time interval 0 – 1450 days after first Biomagnetic Liver Susceptometry. Patient diagnosis: ß-thalassemia major (patient 3,12,13,15), α-thalassemia major (patient 16) and Diamond-Blackfan anemia (patient 7).

In patient 7, 12 and 16 the LIC decreased over the followed time. The diagnosis of these patients were diamond-blackfan, ß-thal major and α-thal major, respectively. In patient 3, 13 and 15, all ß-thal major, the iron level increased more or less.

# 3 Discussion

One advantage of the non-invasive technique of BLS is demonstrated by the fact that in 19 of 23 of our very young patients the biomagnetic measurement could be performed without sedation. The clinical need to know the iron burden in a very young age in the other 4 patients, made it necessary to choose a sedation. Although, sedation is not only a question of age as has been observed in a few patients older than 4 years.
In 19 Patients with LIC >800µgFe/$g_{liver}$ therapeutic intervention by chelation treatment was started after the first biomagnetic quantification of liver iron. In 6 patients the LIC was followed over a time of up to 1450 days. In three of these children the LIC could kept in the recommended rage under 2100 µgFe/$g_{liver}$ after the onset of chelation therapy. In the other 3 patients of this subgroup, the therapy could not be so optimal, that the LIC could lowered to the recommended range.
In 4 patients were we found LIC values between 196 and 469µgFe/$g_{liver}$ (3 sickle-cell disease, 1 rare anemia), no chelation therapy was initiated. But the LIC will be monitored also by further biomagnetic measurements in the future.
To avoid side effects also from chelation therapy, it is planned, to monitor the LIC´s in all patients for the adjustment of the optimal of chelation treatment, because toxicity of the chelation agent increases with the decrease of LIC.
The advantage of the biomagnetic method is, that in all measurements, parents could stay very close to their children, during the examination. For the children, but not less important, also for the parents, the whole procedure was performed without any stress. Both, parents and children realized the conformability of a non-invasive examination.
Due to the precision and the non-invasive character, our results show the benefit of biomagnetic liver susceptometry. The chelation treatment could be adjusted in relation to the liver iron concentration measured. This protects especially the very young children against the potential damage by increased liver iron stores or inadequate chelation treatment.

# 4 Literature


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