Some Aspects of Liver Iron Stores Measurement with the SQUID System

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Abstract. *Direct method of measurement liver iron stores using SQUID gradiometer system is presented. A method for correction of the results, which should be applied depending on the size, shape of the liver and its position against the sensor is given. The possibility of using this noninvasive method in clinical practice is presented.*

Keywords: SQUID Gradiometer System, Liver Iron Quantification, Ferritin

1. Introduction

Iron occurs in the liver in the form of a protein called ferritin. For this reason the liver susceptibility χ differs from the surrounding diamagnetic tissue. In a healthy human body there can be up to 4 g of iron with 400 mg (on the average) of iron storage in the liver [1]. Liver χ varies according to the concentration of iron c_{Fe} (mg_{Fe}/g_{tissue}), and therefore in the magnetic field it results in corresponding change of the liver magnetization M_m. As the measured values of the M_m are very small it is reasonable to use the SQUID system. Our biomagnetic system consists of the RF SQUID, 2nd-order gradiometer, electronic modules, movable patient bed and the magnetization system with Helmholtz coils generating the uniform magnetic field in the direction of gradiometer axis. The magnetization system is driven by AC current [2, 3] with the frequency of 2.8 Hz. The gradiometer measures magnetic induction B_m above the abdomen and it is placed close to the surface near the liver [4].

2. Methods and results

To define the relation between the SQUID gradiometer output voltage U_{pp} and c_{Fe}, the reference phantom of the adult torso has been constructed, Fig 1. The phantom consisted of two acrylic containers filled with distilled water, which simulated a diamagnetic environment of the thorax and abdominal cavity with the volume of 0.023 m^3 and 0.02 m^3, respectively. Inside these containers there were placed two air-filled polyethylene 0.001 m^3 models of lung lobes and cylindrical or ellipsoidal model of liver with volume of 0.001 m^3 filled with the specific aqueous solution of paramagnetic $FeCl_3 \cdot 6H_2O$, where c_{Fe} was ranging from 0.1 - 5 mg_{Fe}/g_{water}. Using this phantom, from four measurements of B_m, the dependence of average c_{Fe} on U_{pp} and the 95% confidence interval for this SQUID biomagnetic system has been determined, Fig. 2. Measurements proved the linear relationship $c_{Fe} = f(U_{pp})$, however, also a relatively large uncertainty in determining the values of low c_{Fe}, which practically makes impossible to distinguish the reduced value of c_{Fe} (iron deficiency) from normal levels (0.1-0.5 mg_{Fe}/g_{tissue}). On the contrary, pathologically high values of c_{Fe}, above 1.5 mg_{Fe}/g_{tissue}, will be determined more reliably. As the mass susceptibility of $FeCl_3 \cdot 6H_2O$ is approximately by one-half less than the mass susceptibility of ferritin ~ 1.6×10^{-6} m^3kg^{-1} [5], the dependence of $c_{Fe} = f(U_{pp})$ derived from the model measurement has been recomputed to the ferritin value, see right axis in Fig. 2. Measurements of c_{Fe} are mainly influenced by i) the position of the gradiometer towards the liver and ii) the volume and the shape of the liver. To enable the

Fig. 1. Configuration of the phantom of thorax and abdomen consists of two containers filled with distilled water, models of lungs and liver. A part of the SQUID system is shown above.

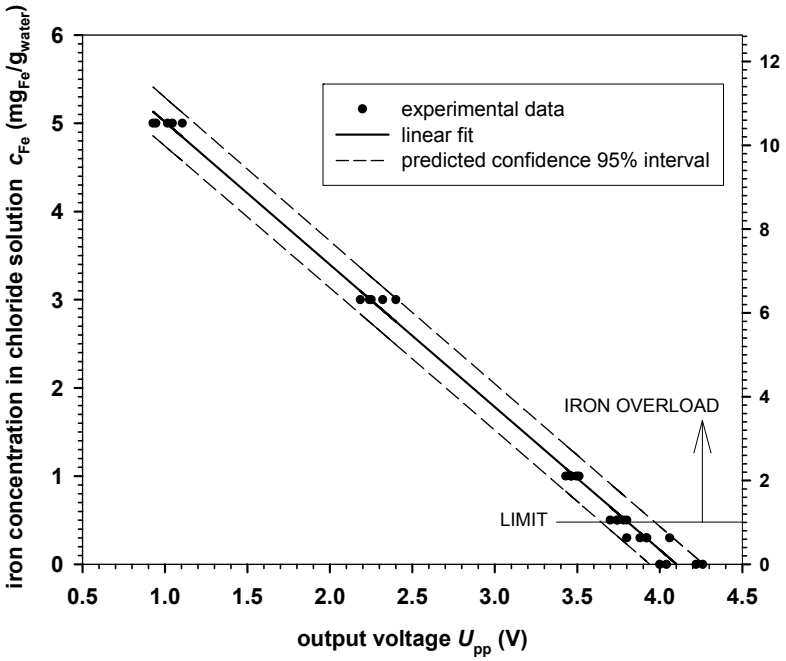

Fig. 2. Correlation between the iron concentration c_{Fe} and output voltage U_{pp} for determining the iron in chloride solution $FeCl_3 \cdot 6H_2O$ and ferritin.

comparing of various measured values of c_{Fe}, the theoretical calculations of B_m have been made: amorphous shape of the liver and middle part of the model were replaced by the defined spherical volumes V_N and using the MR images of the abdominal cavity, these spherical volumes were placed in the nearest position to the gradiometer axis, Fig.3. The measurements demonstrated, that the detection characteristics of the used 2nd order gradiometer is relatively narrow, therefore we estimated that lateral and distant parts of the liver will not significantly affect the overall measured value of B_m. The calculation of B_m also assumes that ferritin is in the liver dispersed homogenously, liver tissues and surrounding diamagnetic tissues have the same properties as water and B_m will be always measured at a distance of 0.01 m from the surface of the model, or the abdomen above the right greater part of the liver.

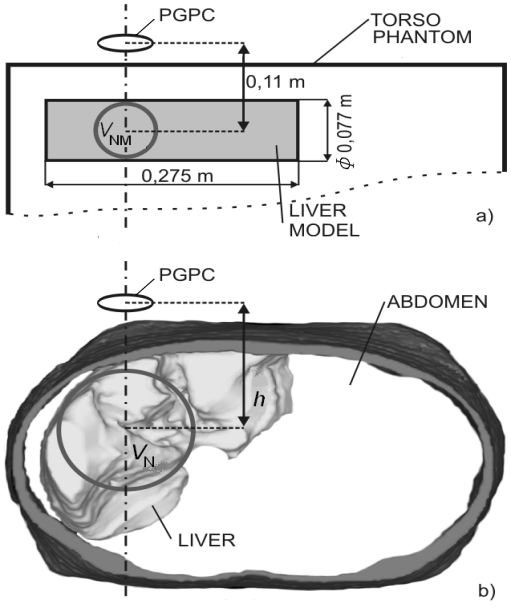

Fig. 3. Approximation of the model (a) and the liver shape (b) by spherical volumes V_{NM} and V_N using MR images of the transversal section of the abdomen, PGPC – proximal gradiometer pick-up coil.

Theoretical calculation B_m comprising the size, shape and position of the liver can be performed if V_N is divided into small elements (with the volume of 10^{-6} m^3) which are located on rings (of the width of 0.01 m) around the gradiometer axis. As all elements have the same magnetic moment $\vec{m}$ oriented in the direction of the magnetic field, values B_m can be calculated consecutively for each of gradiometer coil due to relation [6]

$$\vec{B}_m(\vec{m},\vec{r}) = \frac{\mu_0}{4\pi}\left[\frac{3(\vec{m}.\vec{r})\vec{r}}{r^5} - \frac{\vec{m}}{r^3}\right] \tag{1}$$

where $\vec{r}$ is the position vector of pertinent magnetic element towards the sensing coil. From the nature of relation (1) is clear, that for each of small magnetized element is sufficient to calculate only the variable component, so-called position parameter $A(x,h,ib)$ by formula

$$A(x,h,ib) = \frac{3(h+ib)^2}{\left[\sqrt{x^2+(h+ib)^2}\right]^5} - \frac{1}{\left[\sqrt{x^2+(h+ib)^2}\right]^3} \tag{2}$$

where x is the radius of the rings, h is the vertical distance between the center of V_N and the center of the proximal gradiometer pick-up coil (PGPC), b is the baselength and i = 0,1,2. By summation of all values $A(x,h,ib)$ related to a given V_N, applying to all gradiometer coils, the cumulative positional parameter $A_C(V_N,h)$ for h in the range from 0.08 to 0.22 m and V_N 0.00025 to 0.002 m^3 were obtained, Fig. 4. When the cylindrical model was replaced by the spherical model with V_{NM} = 0.00024 m^3, which was located at the distance of h_M = 0.11 m from the PGPC, the cumulative positional parameter for the liver model $A_{CM}(V_{NM},h_M)$ = 3.15×10^{-7} m^{-3} was calculated.

Then the correction factor k was defined as

$$k = A_C(V_N,h)/\, A_{CM}(V_{NM},h_M) \tag{3}$$

where $A_C(V_N,h)$ is cumulative positional parameter for given h and V_N of the measured liver. Then the actual concentration of iron in the liver, which is corrected to the size, shape and position of the measured liver is $c_{Fek} = k\, c_{Fe}$, where c_{Fe} is determined from the relationship $c_{Fe} = f(U_{pp})$, see Fig. 2, ferritin axis.

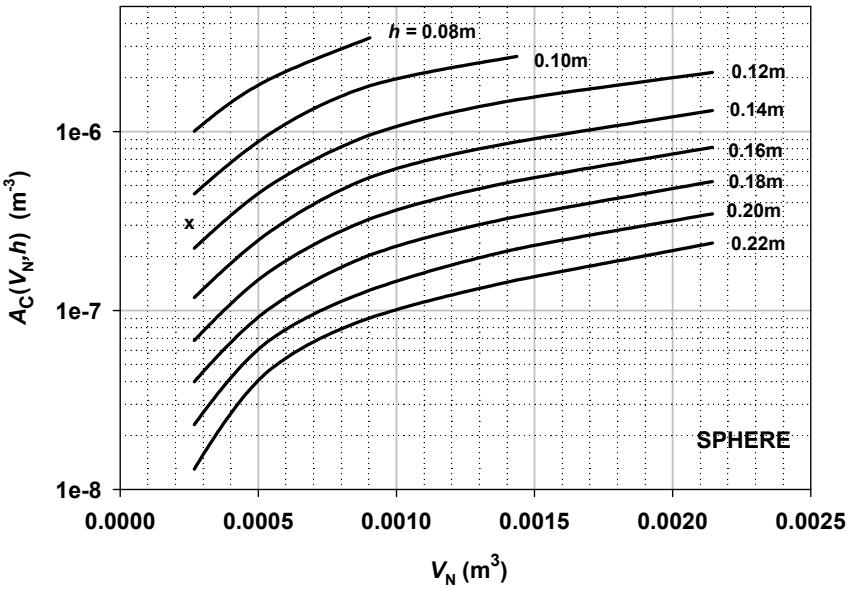

Fig. 4. The cumulative position parameter $A_C(V_N,h)$ depending on the spherical volume V_N and the distance h between PGPC and the center of the sphere. The dagger shows the value of the cumulative position parameter $A_{CM}(V_{NM},h_M)$.

The exact location of the gradiometer above the liver plays an important role, especially regarding repeated measurements. On the liver model with the ellipsoidal shape, the influence of the gradiometer deflection (in two perpendicular directions) on U_{pp} has been studied. Even by change of gradiometer position ± 0.01 m from the center of the ellipsoid, the value of U_{pp} increased by about 13%, what could be eventually rated as a lower c_{Fe} in comparison to reality.

3. Discussion

It is clear that non-invasive magnetometric determination of iron content in the liver is associated with relatively large uncertainties. In order to obtain the relevant c_{Fe} in the liver it is necessary to correct the measured values depending on the position, shape and volume of the measured object. Model measurements showed that we could measure with the uncertainty under 10% only if c_{Fe} is higher than 4 mg_{Fe}/g_{tissue}. A particular improvement of the relative accuracy can be achieved by stabilization of the magnetizing field homogeneity which is affected by temperature changes in the coils of the Helmholtz system. In any case, the decisive influences on the accuracy of measurement liver iron stores are: to find the exact position of the liver to the sensor, and to define the liver volume and its shape.

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