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Peculiar magnetic observations in pathological human liver

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ABSTRACT

DC magnetic measurements confirm presence of (i) diamagnetic, (ii) ferri-magnetic (probably magnetite) and (iii) paramagnetic components in human liver tissues obtained from a normal person and two patients with hematological malignancies. The main observation is that patients' liver tissues show a pronounced magnetic peak at 54(1) K in their zero-field-cooled (ZFC) branches; its origin is not known. One sample shows unusual magnetic features: (i) this peak is irreversible and totally suppressed in the second ZFC sweep, (ii) around the peak position the field-cooled (FC) curve crosses the ZFC one (ZFC > FC). The two phenomena are related to each other.

1. Introduction

Characterization of magnetic properties can offer valuable information for investigations the history and function of materials. Natural systems and diverse biological materials usually contain more than one magnetic component. Even more difficult to characterize are mixtures consisting of different nano-sized magnetic particles. One unusual example of such a complex magnetic mixture is tissues from human liver. Such mixed systems are rarely described, because magnetic measurements of their physical properties are difficult to interpret and various methods of analysis are usually needed to separate and characterize each contributing component. Concerning liver and some other tissues, different magnetic components can be considered as follows. The dominant magnetic signal in human liver arises from the strongly diamagnetic fatty tissue, the matrix in which the other magnetic components are embedded. The second dominant component is ferritin iron core which is responsible for the intracellular storage of iron. Ferritin consists of the nano-sized iron core in the form of ferrihydrite ($5Fe_2O_3 \times 9H_2O$) surrounded with 24 protein subunits [1] which is super-paramagnetic at room temperature. The ferritin structure is very complicated and varies for different organs, animals as well as in normal and pathological cases. The results of various studies of ferritin using electron nano-diffraction, high resolution electron microscopy, magnetization measurements, Mössbauer spectroscopy, etc., demonstrated variability of the iron core structure from one crystallite to many crystallites structure, with surface and internal core regions and/or various layers, with monophasic or multiphase core composition and so on [2–16]. The third dominant component is the ferri-magnetic magnetite (Fe_3O_4) which is magnetically ordered up to 853 K. Magnetite has been discovered in the past decade in human tissues. [14,15,17–20]. The origin and the formation process of this strongly ferri-magnetic component are still unknown and subject of intense research. The fourth dominant component is heme-iron(III) from blood rest in tissues, which is near paramagnetic in its magnetic properties. Here, we present DC magnetic studies performed on normal human liver tissue and on liver tissues taken from two patients with hematological malignancies.

2. Materials and methods

Samples of human liver tissues were obtained post mortem at the Hematological Department of the Sverdlovsk Regional Clinical Hospital No 1 (Ekaterinburg, Russian Federation). Normal liver tissue (assign as N-L) was obtained from a healthy man died after accident. Two pathological liver tissues were taken post mortem from patients with (i) mantle cell lymphoma stage IVB (assign as MCL-L) and (ii) acute myeloid leukemia subtype M4 (assign as AML-L). All liver tissues were washed from blood using

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physiological solution and then lyophilized and powdered.

Magnetization measurements on samples (about 6–14 mg) mounted in gel-caps at various applied magnetic fields (H) in the temperature interval 5 K $< T <$ 300 K, have been performed using a Quantum Design superconducting quantum interference device (SQUID) magnetometer at the "Racah" Institute of Physics, the Hebrew University (Jerusalem, Israel). The differential SQUID sensitivity is 10^{-7} emu. Prior to recording each ZFC curve, the magnetometer was adjusted to be in a "real" $H=0$ state. Then, the samples were cooled to the desired temperatures and the field was switched on to trace the various ZFC branches. The FC branches were measured via worming. Room-temperature (RT) Mössbauer spectra of studied samples (not shown) performed at the Institute of Physics and Technology, Ural Federal University (Ekaterinburg, Russian Federation) by a high velocity resolution spectrometer described in [21], demonstrated typical two peaks spectra due to ferritin-like iron with low absorption effect. The hyperfine parameters deduced are in agreement with all well-known results mentioned above.

3. Results

Comprehensive magnetic measurements have been performed on (i) normal, (ii) mantle cell lymphoma and (iii) acute myeloid leukemia human liver tissues. Generally speaking, the magnetic features of all three samples measured are quite similar to each other. However, the MCL-L tissue exhibits anomalous peculiar magnetic features as shown below. For the sake of clarity, we start with the data measured for N-L sample which also serves a reference material.

Fig. 1 (left inset) shows the ZFC and FC (normalized at 70 K) magnetization curve ($M(T)$) of N-L tissue measured at $H=100$ Oe. The bifurcation below 60 K exhibits the typical behavior of FC > ZFC. The ZFC $M(T)$ curve measured at 1 kOe (the main panel) shows a bulge at 36 K and a kink around 123 K (right inset). This kink may be due to the Verwey transition usually observed for Fe_3O_4, suggesting the existence of tiny amount of magnetite in this normal liver tissue. At low temperatures, the $M(T)$ curves exhibit a typical paramagnetic (PM) shape and adhere closely to the Curie–Weiss (CW) law:

$$\chi(T) = \chi_0 + C/(T-\Theta), \quad (1)$$

where $\chi=M/H$, χ_0 is the temperature independent part, C is the Curie constant, and Θ is the CW temperature. The PM parameters extracted from $M(T)$ (well below 36 K) measured at 1 kOe are: $\chi_0=4.5\times10^{-6}$ emu/g Oe, $C=1.45(1)\times10^{-5}$ emu K/g Oe and $\Theta=1.3(3)$ K. The molecular weight of liver is not known and any estimation of PM effective moment deduced from C is misleading. Since the human liver matrix is diamagnetic [22] this PM type behavior as well as the bulge at 36 K are intrinsic and come from various components exist in the liver tissue.

The isothermal magnetization $M(H)$ curves of N-L sample measured at 25 and 255 K are shown in Fig. 2. These curves can be

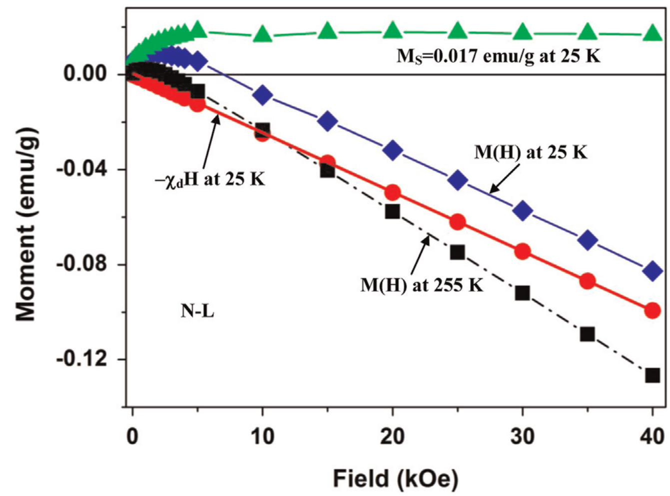

Fig. 2. Isothermal magnetization $M(H)$ plots measured at 25 K (blue) and 255 K (black) for normal human liver (N-L). The linear diamagnetic ($\chi_d H$, red) and the deduced saturation (M_S, green) moments at 25 K are also depicted (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article).

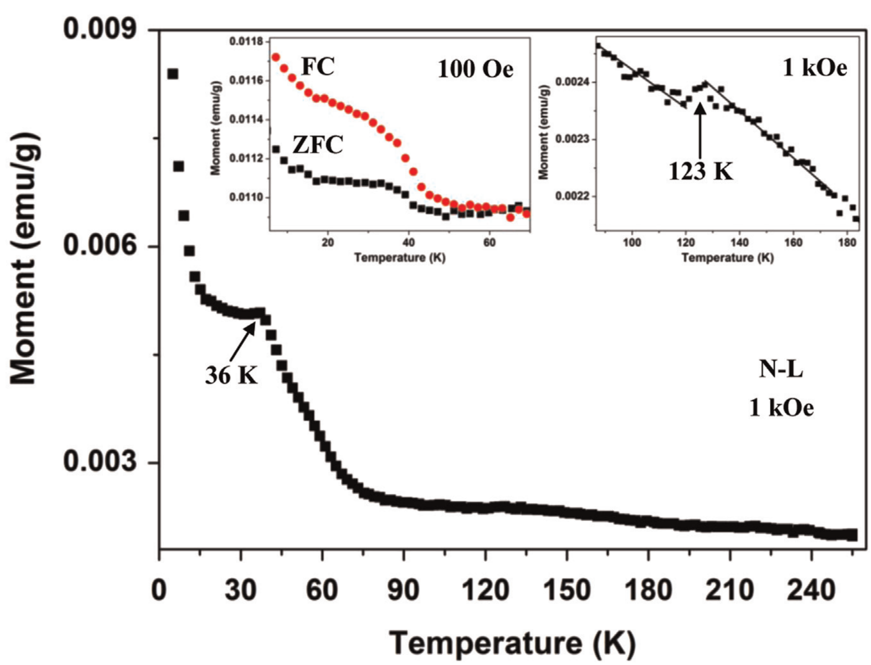

Fig. 1. ZFC magnetization curve of normal human liver (N-L) measured at 1 kOe and the kink observed at 123 K (right inset). The left inset shows the ZFC and FC branches measured at 100 Oe.