

Characterization of the time course of MR relaxation parameters for ageing blood

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Introduction & Theory: Detection of hematomas in subcutaneous and other soft tissues and the estimation of their age are of great relevance in forensic medicine, e.g., for the reconstruction of the sequence of events. Particularly the estimation of the date of origin is difficult as many factors such as skin color, amount of blood and localization influence the external appearance. In MRI, the appearance of extravascular blood depends on the influence of the oxygenation of hemoglobin and its degradation products which affect the relaxation times T_1 , T_2 and T_2^* . The appearance of intracranial hematomas has been well described in literature, and semi-quantitative schemes to stage these bleedings have been proposed [1]. However, a quantitative analysis of the development of relaxation parameters of blood over time at 3T is missing. In this study the aging of blood samples was investigated using quantitative MRI by measuring T_1 , T_2 and T_2^* repetitively over time. A better understanding of the evolution of these parameters may help dating hematomas for forensic as well as for clinical purposes.

Materials & Methods: a) **Blood samples** (3 x 9ml: 2 for MRI (1 test, 1 control), 1 for blood gas analysis) were taken from 6 healthy volunteers (females, males; aged 28-32y) on 3 consecutive days and stored at 4°C to slow down degradation. Prior to MRI the sample tubes were tempered in a water bath to 37°C, and maintained at this temperature during MRI by placing them in a temperature controlled box (circulation of 37°C warm air). Between the individual MRI sequences samples were rotated to minimize sedimentation of the red blood cells.

b) **MRI measurements** were conducted at 3T (TimTrio, Siemens, Erlangen, Germany) with a CP head coil; the sample tubes were placed in parallel to the main field. Measurements were started on the third day, i.e., when the samples were 0, 1, and 2 days old, and performed repeatedly every third day for a total of 30 days yielding a time series covering every day. T_1 was measured using TIR sequences (TR/TE/TI 6000/7.8/400-2800ms), T_2 using a multi SE sequence (TR/TE/contrasts 2000/8.2ms/32), and T_2^* using a FLASH sequence (TR/TE/ α /contrasts 2000/2.5ms/21°/12). T_2^* was measured for each sample separately to avoid mutual influence of the samples by distortion of the B_0 field. Parameter estimation was done using non-linear least squares minimization (Matlab, Natick, USA). Model equations for T_1 and $T_2^{(*)}$ where $S_{IR} = M_0(1 - \exp(-TI/T_1))$ and $S_{ME} = M_0 \exp(-TE/T_2^{(*)})$, respectively.

Results: Qualitatively, the measurements confirm the findings of the literature for intracranial hematomas. Median values of the time course of the relaxation times are shown in fig. 1. T_1 stayed long during the first few days (mean \pm SD, 1600 \pm 100ms), but then decreased while SD increased. Mean T_2 values for fresh blood were 60 \pm 20ms. Soon after blood withdrawal T_2 started to shorten up to reach a minimum after about 16 days (40 \pm 10ms). Then, T_2 rose again to almost its starting value. The time course of T_1 and T_2 of 3 subjects are shown in fig. 2 and already reveal substantial differences between and within the subjects. T_2^* curves were rather flat compared to T_2 , curves starting with a mean of 20 \pm 12.ms and a minimum of 14 \pm 4ms. A quadratic dependence of $R_2^{(*)}$ on deoxygenation could be confirmed (data not shown). The correlations of characteristic curve values in fig. 3 show that time courses of T_1 and T_2 are in fact related. First, higher T_2 values will generally also show a higher decrease and, second, lower minimal T_2 values lead to a lower signal drop in the T_1 course.

Discussion & Conclusion:

The course of relaxation values clearly mirrors the processes on the molecular level of hemoglobin (Hb). T_2 follows a remarkably systematic evolution which in sum can be attributed to two processes: as deoxygenation proceeds T_2 is shortened. When compartmentalization is being lost by cell lysis this shortening is counteracted, and T_2 increases again. Inter and intra-individual variability was quite large. Partly, variability of the results may be due to the handling of the blood samples where not all sample tubes were completely filled and might have had air inclusions. However, the development of the T_1 course is no so clear. The correlations in fig. 3 cast doubt on the proposed mechanism of metHb formation from deoxyHb [1] and rather supports the mechanisms described in [5] where metHb is formed from oxyHb. Low T_2 values, implying low oxygen which mirror low oxygen concentration prohibit the formation of metHb and little T_1 shortening can be observed. In contrast, at high T_2 values enough oxygen is present, metHb can be formed, and T_1 is substantially shortened. In general, our data agrees with other experiments at 3T for T_1 [2,3] and $T_2^{(*)}$ [4], whereas differences in T_2 probably occurred due to the different imaging sequences used. In conclusion, this study gives an important insight in the complex time dependent behavior of blood in MRI. Initial blood oxygenation plays a crucial role in the further time course and has to be known for age estimation of blood. The discovered relations might help to estimate the unknown initial oxygen saturation. However, further investigations and an improvement of measurement techniques are needed to accurately estimate the age of blood in hematomas using relaxation times.

Refs: [1] William G, Bradley J. Radiology 1993;189:15; [2] Lu H et al. MRM 2004;52:679; [3] Silvennoinen MJ et al. MRM 2003;49:568; [4] Zhao JM et al. MRM 2007;58:592; [5] Faivre B et al., Artif Cells Blood Substit Immobil Biotchnol, 1998, 26:17-26

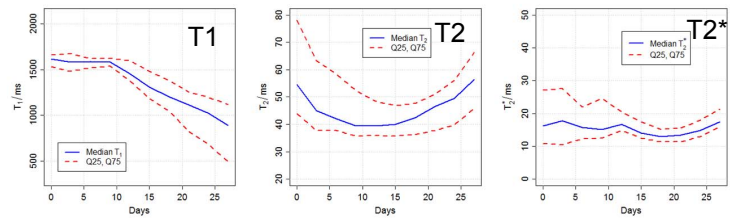


Fig. 1: Median course of T_1 , T_2 and T_2^* over time (quantiles in red).

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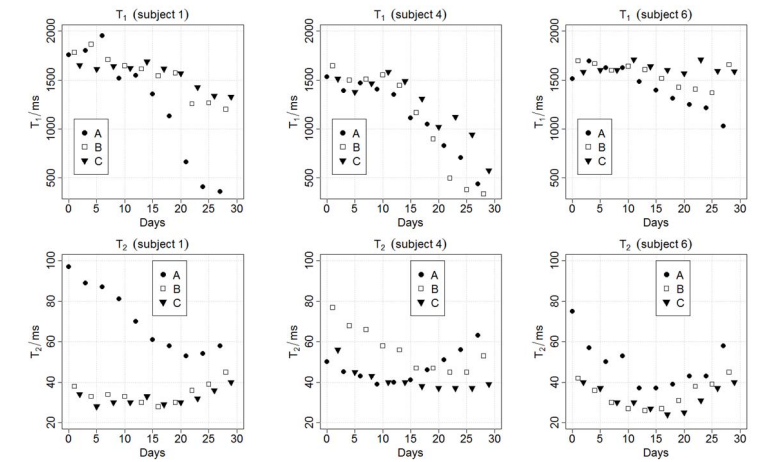


Fig. 2: Time course of T_1 and T_2 for 3 different subjects. Each plot contains 3 different samples (A,B,C).

$$T_2 \text{ diff} = T_2 \text{ start} - T_2 \text{ min}, T_2 \text{ mean} = (T_2 \text{ start} + T_2 \text{ min}) / 2 \quad T_1 \text{ diff} = T_1 \text{ start} - T_1 \text{ end}$$

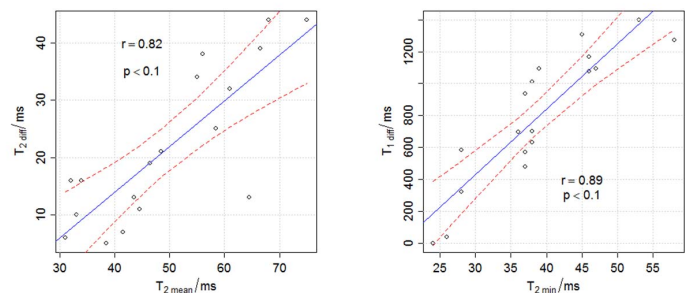


Fig. 3: Correlations of starting and minimum T_2 values (left) and minimum T_2 and start to end T_1 difference.