Assessment of Iron Concentration in a Two-Pool Model of Brain Tissue

C. Langkammer[1,2], T. Seifert-Held[1], M. Soellinger[1], C. Enzinger[1], F. Fazekas[1], R. Stollberger[2], and S. Ropele[1]

[1]Department of Neurology, Medical University of Graz, Graz, Austria, [2]Institute of Medical Engineering, Graz University of Technology, Graz, Austria

1. Introduction

Increased levels of ferritin in various gray matter structures of the brain have been reported for several neurodegenerative diseases including Parkinson's and Alzheimer's disease [1]. Current approaches of quantifying iron content are mainly based on relaxivity effects of iron, providing relaxation rates which are assumed to correlate with the iron content. So far, validation of these methods has been limited to phantoms containing iron compounds other than the brain tissue storage protein ferritin or by referring to the findings of an older histopathological correlation study [2]. However, the latter approach does not allow studying the effects of age, gender, and disease on iron accumulation. Based on the direct saturation technique [3,4], we therefore investigated the saturation line shape of water and its changes due to varying concentrations of iron. We particularly focused on relaxation characteristics expected for brain gray matter, by embedding different concentrations of ferritin in a two-pool model consisting of cross-linked bovine serum albumin.

2. Materials and Methods

Bovine serum albumin (diluted to 0.2 BSA per weight) was cross-linked after adding Ferritin from horse spleen (Fluka, Switzerland, Product-No. 96701) as proposed in [5] to obtain samples of variable ferritin concentration (0, 1, 2.5, 5, 10, 15, 20 and 30 [mgFe/100g sample]). The resulting phantom covered the range of ferritin values published for brain tissue [6] and allowed to consider magnetization transfer effects in white and gray matter [7]. The resulting bound pool fraction was approximately 7%. All measurements were carried out on a 3T scanner (Tim Trio, Siemens Healthcare, Erlangen, Germany). T_1 was determined by using an inversion recovery sequence with multiple inversion times. Direct saturation images were acquired with a spoiled FLASH sequence (TR/TE/FA=70ms/5.44ms/70°), performed with a Gaussian saturation pulse. To investigate the impact of MT and T_1 related effects, identical measurements were performed with a TR of 5s where we assumed MT to be negligible. The saturation pulse had a variable duration (4, 8, 16 and 32ms) and a flip angle of 90°. Following the sweep over 25 different resonance offsets linearly spaced around the resonance frequency of water (step width 30Hz, -360Hz to 360Hz), we also acquired a reference image without the saturation pulse. The saturation measurements were normalized by dividing the off-resonant images by the reference image. A Lorentzian line shape was fitted into the saturation profile yielding the susceptibility induced shift of the resonance frequency, the full width at half maximum (FWHM) and a direct saturation ratio (DSR), i.e. the maximum saturation effect.

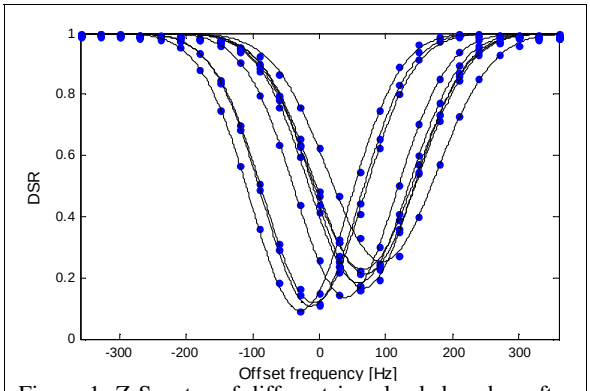

Figure 1: Z-Spectra of different iron loaded probes after applying a saturation pulse with t_s=8ms.

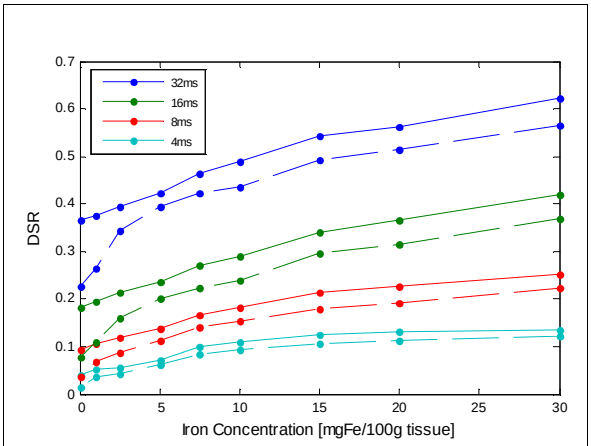

Figure 2: Iron concentration vs. DSR with varying pulse duration (dotted lines the short TR measurements)

3. Results

The relaxation time measurement yielded a T_1 of 1120 ms for the native BSA. Together with the bound pool fraction, this closely resembles gray matter values reported for 3T [8]. DSR measurements with the short TR scaled with the iron concentration, but demonstrated a non linear relationship for lower concentrations (<5mg/100g). This effect has been related to MT recently [3]. In contrast, saturation measurements with long TR revealed a linear relation over the entire range of iron concentrations, with longer saturation pulses resulting in higher sensitivity. The FWHM yielded only small dependency on iron concentration.

4. Discussion/Conclusion

In the presence of MT and susceptibility effects, a condition more realistic for in vivo conditions, the DSR seems to represent a sensitive, linear measure for iron deposition in tissue. Our results emphasise the importance of an appropriate model for mimicking brain tissue. Future efforts will be dedicated to further optimization of this method and subsequent application in vivo.

References:

[1] Berg D, 2006, Topics MRI, 17:5-17, [2] Hallgren B, 1958, JNeuochem, 3:41-51, [3] Zurkiya O, 2006, MRM, 56:726-32, [4] Smith S, 2008, Proc. ISMRM 16th, 884, [5] Koenig S, 1993, MRM, 29:311:16, [6] Haacke EM, 2005, MRI, 23:1-25, [7] Graham SJ, 1997, JMRI, 7:903-912, [8] Sled JG, 2001, MRM, 46: 923-32