Assessment of Iron with 8T MRI T2 Imaging in Human Brain

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INTRODUCTION

The distribution of iron-based proteins varies throughout the brain with aging [1] and is altered in neurodegenerative disorders such as Alzheimer's and Parkinson's disease. Iron-based proteins provide essential redox chemistry sites for metabolism within the brain, and iron catalysis of free radical production is thought to be one of the implicating factors in the onset of Alzheimer's disease [2]. Thus a non-invasive method for assessment of tissue iron would be an important diagnostic tool. Non-heme iron proteins contribute to susceptibility effects that produce local magnetic field changes. The sensitivity to such susceptibility effects with ultra-high field (≥7T) gradient echo (GE) imaging has been well demonstrated; however, GE images are impaired by air/tissue susceptibility artifacts. The objective of this work is to quantify mesoscopic susceptibility effects in ultra-high field using spin echo (SE) images. This is expected to aid in the understanding of ultra-high field T2 contrast mechanisms in normal brain and in the development of diagnostic tools for assessment of neurodegenerative disease.

METHODS

Signal decay in Hahn spin echoes is not only due to the intrinsic T2, but is further increased due to molecular diffusion in an inhomogeneous magnetic field. This latter effect is reduced in CPMG sequences by design. Signal decay for both Hahn and CPMG can be described by a combined expression [3]

$$S=S_0\exp\{(-t/T2)-(\gamma^2G^2Dt^3)/(12n^2)\}$$

where T2 is the intrinsic T2, t=TE/2 and n=1 for Hahn, and t=τ and n=echo number for CPMG. The term γ^2G^2D describes the intra-voxel dephasing due to local (mesoscopic) susceptibility fields from paramagnetic iron particles. Hahn and CPMG images were acquired at different TE for a suspension of iron oxide particles, and on 12 unembalmed, postmortem cadavers (4 autopsy confirmed Alzheimer's, 6 other brain diseases, 2 without known brain abnormality, 4 male, 8 female, ages 57-93). Iron oxide image parameters included six Hahn SE images with TR/TE/NEX=3000ms/15,30,45, 60,120, 240ms/1 and 16-echo CPMG with TR/τ/NEX=3000ms/15ms/1, single slice, FOV=16x12cm, matrix=256x192. Cadaver images included four Hahn SE images with TR/TE/NEX=1500ms/21.7,50,90, 134.4ms/2 and 8-echo CPMG with TR/τ/NEX=1500ms/12.7ms/2, single slice, FOV=16cm, matrix=512x384, and final resolution of 312x312x3000μm^3. A nominal 90° flip angle was determined near the hippocampus using a voxel selective stimulated echo spectroscopy sequence, local flip angles were measured [4] and varied across the image by more than two-fold. Hahn and CPMG data were fitted individually to a mono-exponential decay, as well as with the combined equation using IDL.

Following removal of the brain at autopsy, tissues from regions within the imaged slice were collected and placed in methanol for histological staining. Adjacent tissues (50-100mg) were collected for measurement of total tissue iron by mass spectroscopy, dissolved in 3mL concentrated HNO_3, and prepared by microwave digestion on an Ethos Advance Microwave Labstation. Finally, mass spectroscopy measurements for isotopes ^{56}Fe and ^{57}Fe were made on a ThermoFinnigan Element 2.

RESULTS

Images with TE≥50ms demonstrate gray matter (GM) with lower signal than white matter (WM). Example intrinsic T2 and γ^2G^2D images for an Alzheimer's case are shown (color scale: 0-150ms for the T2; 0-6·10^{-5}ms^{-3} for γ^2G^2D). The intrinsic T2 values were only slightly shorter for GM than WM, whereas γ^2G^2D values were significantly higher for GM. Highest γ^2G^2D values were observed for the high iron-content nuclei and lowest values for CSF. Also shown are histograms of γ^2G^2D values for GM of the frontal gyrus and for adjacent WM. Grey matter γ^2G^2D values for normal brain are substantially shifted toward higher values compared to Alzheimer's brain indicative of increased iron content. For the iron oxide samples, correlation between iron content with γ^2G^2D demonstrated a quadratic behavior (Figure 3b). Brain tissue γ^2G^2D versus total iron content (Figure 3A) for GM and WM showed similar behavior.

DISCUSSION AND CONCLUSION

Our analysis clearly shows that susceptibility effects play a dominant role in SE ultra-high field MRI. Combined fitting of Hahn and CPMG spin echoes provides a sensitive, non-invasive measure of tissue iron content. This method may prove useful for in-vivo study of iron content in normal aging and neurodegenerative diseases such as Alzheimer's. Though the current image acquisition protocol is too long for imaging cognitively impaired patients, some preliminary data have been collected on in vivo in healthy subjects indicating similar contrast patterns to those observed in our postmortem studies. Various approaches for shortening scan time are under investigation.

REFERENCES

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