Simultaneous Imaging of Myelin and Iron using Ultrashort Echo Time (UTE) MRI

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Target Audience: Neuroradiologists, Neurologists, and Multiple Sclerosis Investigators

Purpose: Imaging of iron in the central nervous system (CNS) has been the subject of intensive investigation. Iron deposition is increased in the subcortical gray matter in a number of conditions including multiple sclerosis (MS)[1]. We have previously reported on the use of an inversion recovery ultrashort echo time (IR-UTE) pulse sequence to image myelin in the central nervous system[2,3]. This method utilizes an inversion pulse to null the signal from longer T2 protons based on their T1 time. In this study, we exploit the increased relaxivity of tissue produced by iron to simultaneously image myelin and increased iron in the brains of MS patients and cadaveric donors with MS. We also explore the mechanism by which the IR-UTE pulse sequence is able to detect myelin and iron deposition.

Methods: All imaging was performed on a Sigma HDx 3T Scanner (GE Healthcare, Milwaukee, WI). An adiabatic inversion recovery (IR) pulse was used to invert the longitudinal magnetization of long T2 tissue components (**Figure 1**). The UTE data acquisition began after the delay time (TI) at which the inverted longitudinal magnetization of the long T2 components in white matter reached the null point. Short T2 components were saturated and recovered during TI. These were subsequently detected by the 2D UTE data acquisition. Typical imaging parameters were: TR 1500ms, FOV = 24 cm, Matrix =256x256, Bandwidth = 125 kHz, TE = 0.01 ms 2.2 ms, 5ms, 7.5 ms; TI varied between 100 – 500 ms and was chosen to optimize long T2 component nulling. Image analysis was performed in ImageJ and Matlab using custom scripts for as described previously[2].*Myelin Phantom Preparation*: A 520 mg synthetic myelin lipid phantom approximating the nonprotein portion of biological myelin was prepared and consisted of 50% (w/w) (D2O), 13.5% cholesterol, 13% galactocerebroside, 19.3% phosphatidylcholine, and 4.2% sphingomyelin (Sigma-Aldrich, St. Louis, MO) using a previously described procedure[4].*Iron Phantom Preparation:* Feridex solutions were prepared at a variety of concentrations and placed in small tubes embedded in an agarose medium to minimize magnetic susceptibility differences.

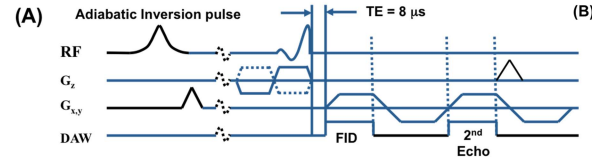


Fig 1 (A) IR-UTE sequence employs half pulse excitation and dual echo radial ramp sampling preceded by an adiabatic IR pulse to invert and null the long T2 white matter. (B) Signal of myelin and tissue affected by iron recover during TI.

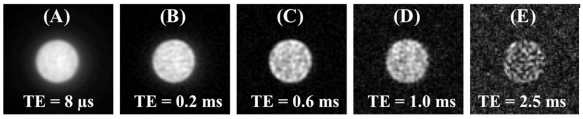
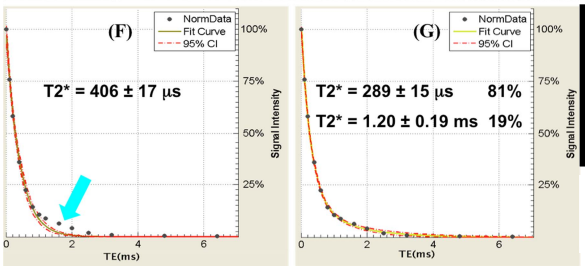


Fig 2 Synthetic Myelin Phantom consisting of lipids and D2O (50% w/w). Fitting of IR-UTE MRI signal versus TE shows two components with T2* times of 1.2 ± .2 ms and 290 ± 20 µs.



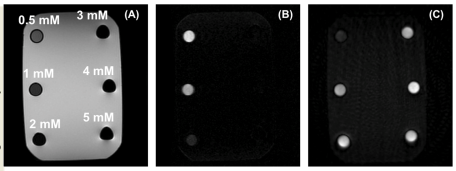


Fig 3: Ferridex Phantom. A) Spin echo. B) MP-RAGE shows no signal for > 3 mM. C) IR-UTE shows signal from all concentrations.

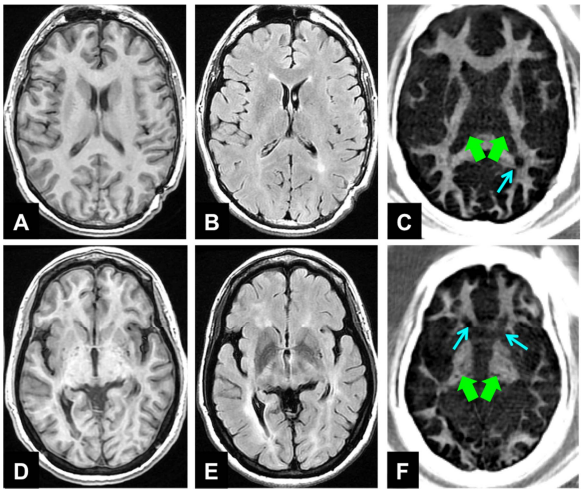


Fig 4 (A-C) 37 yo male with MS, (D-F) 43 yo female with MS (A&D) T1 3D GRE: TR 8 ms, TE 3 ms, 512x 512 FOV 25 cm, FA 12 ST 3 mm (B&E) T2 FLAIR: TR 9502, TE 124.30, 512 x 512, FOV 25 cm, FA 90 ST 3mm. (C&F) IR-dUTE: TR 1000, TI 320, TE 0.01 ms – 2.2 ms, FA 60, FOV 25 cm, 256 x 256 ST: 5 mm. IR-UTE MRI shows higher intensity signal in F which is not seen in a similar region of the patient in B (Thick Green Arrows). This may represent iron deposition in the area of the thalamus. Thin blue arrows point to MS lesions.

Results:
Figure 2 shows UTE MRI images of the myelin lipid phantom in D2O. Exponential fitting demonstrates two ultrashort components with T2* times of 1.2 ± .2 ms and 290 ± 20 µs. **Figure 3** shows a Feridex iron phantom with all concentrations detected by IR-UTE MRI compared MPRAGE. **Figure 4** shows

Discussion: There has been debate about whether the ultrashort T2 signals found in the brain are from myelin directly or myelin associated water. Others have previously shown in spectroscopy experiments that this signal is preserved in the presence of D2O[5]. We show here that an ultrashort T2 signal is detected in D2O with MRI and contains potentially two components. This suggests that the signal source is the myelin lipid protons and not myelin associated water. We also show that IR-UTE sequences generate a positive signal and are sensitive to higher concentrations of iron compared to MPRAGE. Combining these concepts allow us to simultaneous detect white matter abnormalities and presumed iron deposition in patients with multiple sclerosis. With IR-UTE sequences significant iron deposition will appear high signal and white matter MS lesions will appear low signal in a single scan.

Conclusions: Ultrashort T2* signals from myelin detected by IR-UTE are preserved even in D2O. IR-UTE sequences are sensitive to a wide range of iron concentrations. IR-UTE offers dual sensitivity to myelin lesions and iron deposition in the CNS.

References:

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