

# Simultaneous Quantitation of T<sub>2</sub> and Concentration of vitamin C and GSH in the Human Brain In Vivo Using Multiple Echo Time Double Editing With MEGA-PRESS at 4 and 7 T

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## Introduction

Noninvasive methodology for quantifying antioxidant concentrations in human tissue would be useful to study diseases that are known to involve oxidative stress. Vitamin C (ascorbate) and glutathione (GSH), the two most concentrated chemical antioxidants in the CNS can be detected using double editing with (DEW) MEGA-PRESS (1). For quantitation from spectra at the long TE characteristic of edited spectroscopy, influence of T<sub>2</sub> on resonance intensity is typically assumed constant across study populations. However, the following method for simultaneously measuring antioxidant concentrations and T<sub>2</sub> was developed to increase the certainty with which differences in antioxidant signals can be attributed to changes in concentration.

## Methods

Although editing efficiency is optimal at one TE due to J-coupling, appreciable signal can be detected at sub-optimal TE. DEW MEGA-PRESS spectra (1) were measured at 4 (TR = 4.5 s) and 7 (TR = 5 s) Tesla from solutions of ascorbate (Asc) and GSH. Appreciable resonances were observed at several TE at both field strengths. DEW MEGA-PRESS spectra identified as such were measured in the human occipital cortex (4 and 7 T) using a surface coil. At 4 T, spectra were measured at several TE (NEX = 96 per TE) in 22 subjects. At each TE, spectra were summed over all subjects. To account for resonance intensity changes arising from J-modulation, Asc and GSH resonances were normalized to spectra simulated using density matrix formalism and apodized to mimic in vivo line widths. T<sub>2</sub> were calculated from normalized areas under the edited Asc and GSH resonances according to  $A = A_0 e^{-TE/T_2}$ . To study the impact of co-edited resonances from PC, GPC, Ins and NAA on integrated peak areas, contributions from these compounds were simulated.

## Results

Fig. 1 illustrates that at 4 T, appreciable Asc and GSH resonances can be detected at several TE in the human brain. Simulated and measured solution spectra matched. Fig. 2 plots the normalized areas under the Asc and GSH resonances in the spectrum summed over 22 subjects at 4 T and T<sub>2</sub> fits. Table 1 reports corresponding T<sub>2</sub>. Confidence in the short GSH T<sub>2</sub> is substantiated by the small GSH resonance at 152 ms TE in vivo (fig. 1). Confidence in the T<sub>2</sub> measured for Asc was low, as expected given the poor fit (fig. 2). Simulated spectra evidenced contamination of the Asc resonance by co-edited PC, GPC, and Ins at physiologic concentrations, putatively compromising the T<sub>2</sub> measurement. Fig. 3 illustrates that at 7 T, appreciable Asc and GSH resonances can be detected at several TE in solution and in the human brain.

## Discussion

To our knowledge, this is the first time the T<sub>2</sub> of GSH has been reported and edited GSH detected at > 4 T. The GSH T<sub>2</sub> was measured with practicable certainty in the human brain at 4 T. Detrimental influence of co-edited resonances on the Asc resonances measured at 4 T motivated attempts to fit via LCModel. Unfortunately, absence of macromolecule basis spectra and inconsistency in the spline baseline were problematic. Plausibility for measurement of Asc T<sub>2</sub> at 7 T is likely due to: minimal co-editing via increased spectral dispersion, shorter TE via shorter editing pulses and sensitivity gains.

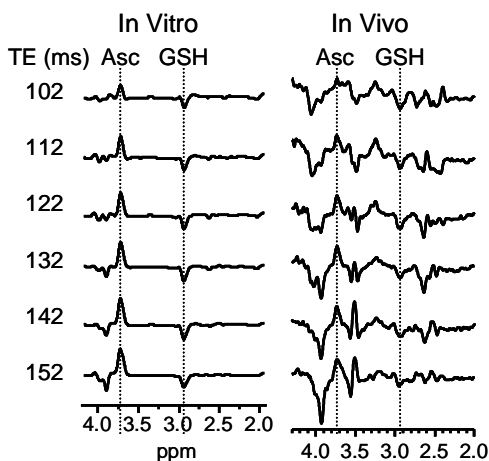


FIG. 1 DEW MEGA-PRESS edited spectra measured at 4 T. VOI = 27 mL.

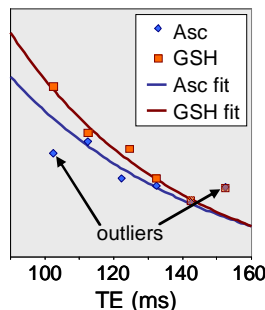


FIG. 2 Areas under resonances and T<sub>2</sub> fits.

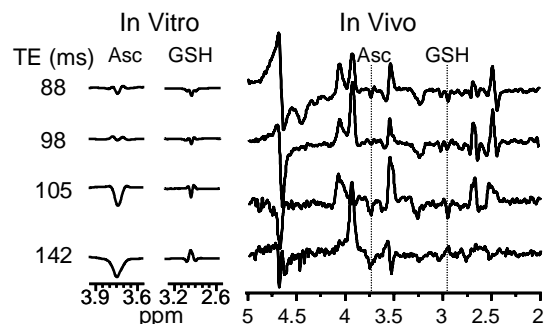


FIG. 3 DEW MEGA-PRESS edited spectra at 7 T. VOI = 8 mL, NEX = 256.

Table 1. T<sub>2</sub> (ms) and confidence intervals

	T <sub>2</sub>	low 95% CI	high 95% CI
Asc	57	32	268
GSH	50	41	62

Ref. 1) Terpstra et al. *Magn Reson Med* 56:1192 2006.

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