Examining saturation corrections for in-vivo liver ^{1}H-MRS glycogen measurements in a clinical 3T scanner

Ronald Ouwerkerk[1]

[1]*Biomedical and Metabolic Imaging Branch, NIH/NIDDK, Bethesda, MD, United States*

Introduction

Understanding the regulation of glucose storage in glycogen is a crucial element for uncovering the cause of metabolic diseases such as obesity or diabetes type II. Glycogen can be observed with ^{1}H-MRS in the liver and in vivo T2 were reported (1). However, concentrations measured with ^{1}H-MRS (1) are lower than reported for biopsy (2) or ^{13}C-NMR (3). Possible error sources are the correction factors for relaxation of glycogen or water. The relaxation of glycogen has been extensively studied at high field (4), but not with sequences and field strength that were used for in-vivo measurements in humans. Signal variations as a function of TE are subject to coupling effects. Because those variations can be very sequence specific glycogen samples were characterized with T_2 measurements and varying echo spacing using the same equipment and PRESS sequence used for in-vivo measurements of glycogen in human liver. Additionally T_1 measurements were performed with a STEAM sequence.

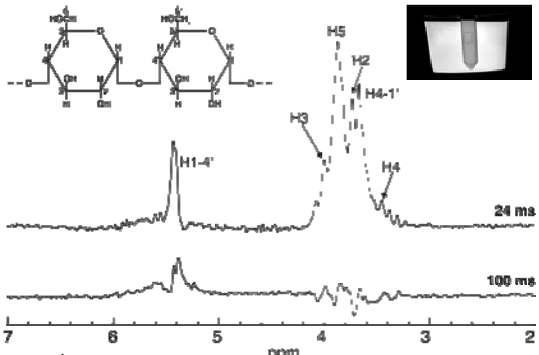

Fig. 1 *^{1}H-MRS of a glycogen phantom at 37ºC recorded with 8ml volume PRESS at 3T with TE 24 and TE 100ms. The inserts show the structure of two glucosyl units (top left) and axial scout image of the water bath and sample tube (top*

Materials and Methods

Single volume PRESS scans were performed on a Siemens Verio 3T MRI scanner with 2x2x2cm single volume PRESS (5) at TR=6s. Glycogen phantoms were prepared with bovine glycogen (Sigma_Aldrich, St. Louis, MO). Glycogen was dissolved in a potassium chloride and phosphate buffer (KCl: 110 NaCl 10, K_2HPO_4: 7, KH_2PO_4: 3 mmol/l, pH 7.14 at 37º). Glycogen from two different batches was used. Both had to be dialyzed against the buffer solution to remove residual ethanol. Hence, the final concentrations could only be estimated by MRS using the method in ref (1). Two dilution series (1:2, 1:3 1:10) were from stock solutions with 172 and 260 mmol/l glucosyl unit concentration. Plastic centrifuge tubes with 50ml of these solutions were immersed in a 3 liter insulated water bath (see fig 1 insert), kept between 38º and 36º C. For the most concentrated glycogen sample the T_2 was measured with water suppression. The T_2 and T_1 of water were measured on all samples without water suppression. Time domain signals were fitted with AMARES (6) to Gaussian line phases of all signals constrained to the fitted zero-order phase. T1 of water was estimated from the signal ratios of unsuppressed spectra at TR 6 and TR 24 via a lookup table. T1 of glycogen was determined with a STEAM sequence on the 172 mmol/l sample by varying the mixing time between 10 and 100ms.

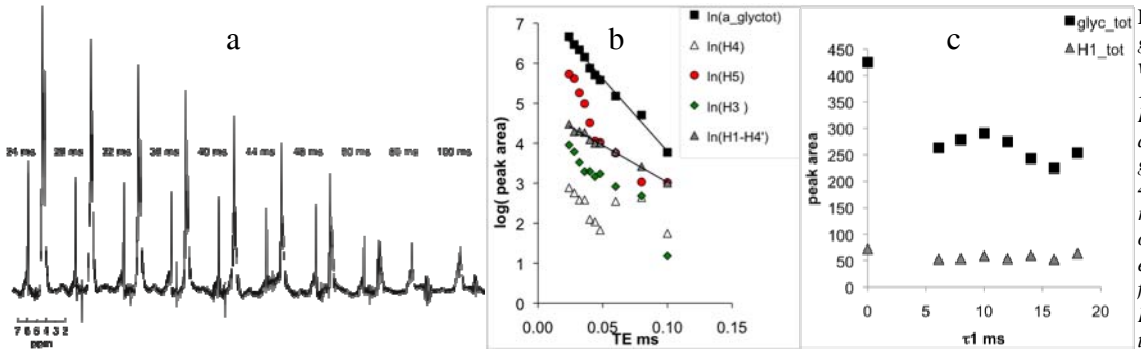

Fig. 2. (a) *T_2 measurement of a glycogen phantom. Expanded version of the spectra at TE 24 and 100ms shown in fig1. (b) Logarithmic plot of fitted peak areas with linear fit of the summed glycogen peaks between 3.5 and 4.2ppm (a_glyctot) and H1 resonance at 5.28 ppm. (c) Signal changes as a function of PRESS echo spacing $\tau 1$ = time from 90 to first 180 with fixed total TE = 48. Points at $\tau 1$=0 were measured at the minimum TE=24.2 ms.*

Results and discussion

The signal from the glycogen H1 varied exponentially as a function of TE. Linear regression of the log of the peak areas vs. TE yielded a T_2 of 54 ms with r2=0.99 (see fig. 2b) in the most concentrated sample (260 mmol/l). The individual signals of the other glycogen protons (H3, H4 and H5 3.5-4.2 ppm) do not appear to be decaying in an exponential manner. Even so, linear fit of the summed peak areas yielded an apparent T_2 of 22 ms (r2=0.95). PRESS spectra with a constant total TE of 48 ms and varying the echo spacing showed a coupling effect (fig 2c). Thus, the signal correction of these H3,H4 and H5 peaks using an exponential model with TE=22ms is not accurate. Data collected with the minimum TE of 24.2 ms are also shown in fig 1c at $\tau 1$=0. When both TE 24 and TE 48 data are T_2 corrected using exponential model with T_2=22ms the corrected signals for TE 24ms are about 50% lower than those predicted from signals measured TE 48 ms. Thus is would seem that the echo spacing at minimum TE causes signal loss through coupling effects. The back extrapolated values for TE=0 from signals at TE 24 and 48 for the H1 proton, on the other hand, agree within 5%.

The apparent T_1 of the group between 3.5-4.2ppm and of the H1 proton are similar, both 159 ms with non-linear fit or 152 and 148 ms respectively with linear regression on log data. The T_2 relaxation of the water in the dilution series varied with glycogen concentration. The R_2 of water varies linearly with glycosyl unit concentration (fig 3). This may well be a result of chemical exchange between glycogen (H1 proton) and water. The T_1 for water decreased from 3.25 to 2s with increasing glycogen concentration.

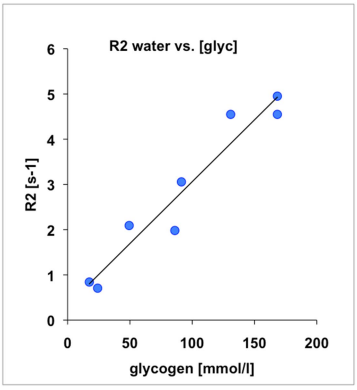

Fig. 3. (a) *The R2 of water in the glycogen samples a s a function of glycogen (glycosyl unit) concentration.*

Conclusion: Coupling effects influence the glycogen signal strength as a function of TE. Better correction factors or optimized TE and echo spacing would improve the accuracy of in vivo measurements of glycogen with ^{1}H-MRS. Alternatively a gold standard calibration could be used as long as correction for water T_2 relaxation is applied.

References:

1. Ouwerkerk R, Pettigrew RI, Gharib AM. Radiology 2012;265(2):565-575.
2. Nilsson LH, Hultman E. Scand J Clin Lab Invest 1974;33(1):5-10.
3. Rothman DL, Magnusson I, Katz LD, Shulman RG, Shulman GI. Science 1991;254(5031):573-576.
4. Chen W, Avison MJ, Zhu XH, Shulman RG. Biochemistry 1993;32(43): 9417-9422.
5. Bottomley PA. Ann N Y Acad Sci 1987;508:333-348.
6. Vanhamme L, van den Boogaart A, Van Huffel S. J Magn Reson 1997;129(1):35-43.