Glycogen chemical exchange effects in ^{1}H-MRS and glyco-CEST at 3T and 7T

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Introduction

Understanding the regulation of glucose storage in glycogen is a crucial element for uncovering the cause of obesity or diabetes type II. Glycogen is can be observed with ^{1}H-MRS in the liver(1), or with (^{1}H) CEST-MRI in muscle (2). However, concentrations measured with ^{1}H-MRS (1) are lower than reported for biopsy (3) or ^{13}C-NMR (4). The chemical exchange mechanism that is the basis of glycoCEST (5)could reduce the glycogen signals in water-suppressed ^{1}H-MRS. We investigated the effect of water suppression (WS) RF power on 1H-MR spectra of glycogen phantoms using the exact sequence used for in-vivo ^{1}H-MRS quantification of glycogen in the human liver(1). The effect of water suppression offset was examined using the z-spectra of glycoCEST on a series of phantoms with varying glycogen concentrations in physiological buffers.

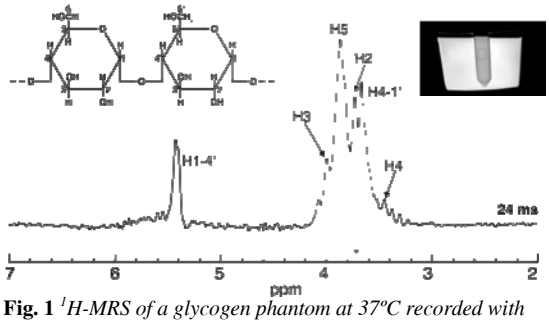

Fig. 1 *^{1}H-MRS of a glycogen phantom at 37ºC recorded with 8ml volume PRESS at 3T with TE 24 and TE 100ms. The inserts show the structure of two glucosyl units (top left) and axial scout image of the water bath and sample tube (top*

Materials and Methods

Single volume PRESS glycogen spectra were recorded on a Siemens Verio 3T MRI scanner with 2x2x2cm single volume PRESS (6) at TR=6s as described in ref (1). Glycogen phantoms with seven different glycogen concentrations were prepared from two separate batches of Bovine glycogen (Sigma_Aldrich, St. Louis, MO). The samples were 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) and dialyzed against this solution to remove residual ethanol. Plastic centrifuge tubes with 50ml of these solutions were immersed in a 3 liter insulated water bath, kept between 38º and 36º C. The RF power on all WS pulses was varied between 0 and three times the optimum WS power setting and both residual water and glycogen signals were quantified. Time domain signals were fitted with AMARES (7) to Gaussian line phases of all signals constrained to the fitted zero-order phase. Glycogen concentration was calculated from the summed area of nine fitted resonances in the area between 3.5 and 4.2 ppm and corrected for T_2 relaxation of water and glycogen as described in (1). Glyco-CEST images were recorded on a Philips 7T scanner using a train of ten 50 ms Gaussian pulses at 2 µT power level. The saturation pulse was applied from -5 ppm to 5 ppm in 59 steps plus one unsaturated image. The z-spectra were corrected for water resonance offset. The MTRasymmetry was quantified by subtracting the downfield side from the upfield side. The glycoCEST signal was taken as the signal at 0.9 ppm in the MTR asymmetry.

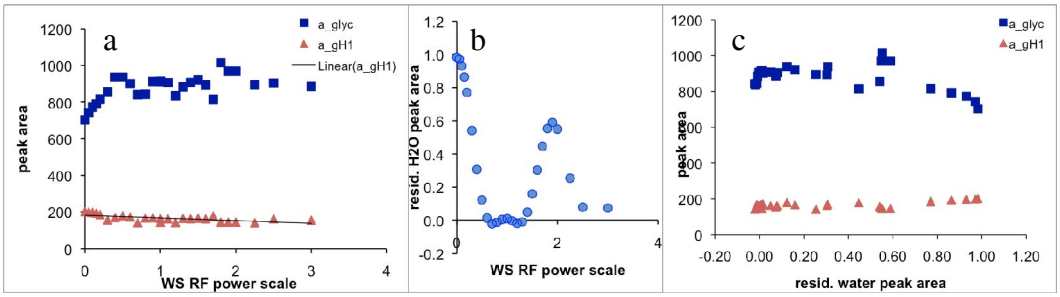

Fig. 2. *Effect of WS RF power on the glycogen and water peak areas in a glycogen phantom spectrum at 37ºC. a) The glycogen peak areas as a function of RF power scale (relative to optimum power) b) The residual water fraction vs. WS RF power scale. c) Glycogen peak areas vs. residual water. Red triangles are the peak area of the (exchanging) H1 protons. The dark blue squares are summed areas of peaks between 3.5- 4.2 ppm.*

Results and discussion

Varying the water suppression power showed a light decrease of the H1 proton signal with increasing water saturation power (fig 2). The summed signals of the other glycogen protons could not be accurately quantified in the presence of large residual water peaks as found with RF power scale below 0.5 and around 2. Quantification of these peaks with AMARES was hindered by vibration artifacts spurious echo signals and rolling baseline. These signals did not appear to diminish at higher water suppression powers. Thus, quantification based on the peaks in the 3.5-4.2 ppm region is hardly affected by water suppression power settings. It is also clear that using spectra without water suppression is not a good option unless the water signal and associated artifact is avoided by other means. The glyco-CEST experiments showed no concentration dependent effects downfield, whereas the MTR asymmetry correlated with the MRS estimated concentrations. MRS can complement glyco-CEST in providing information about local glycogen concentrations. Both methods can and should be used to study glycogen metabolism until more is known about spatial variations of glycogen deposits.

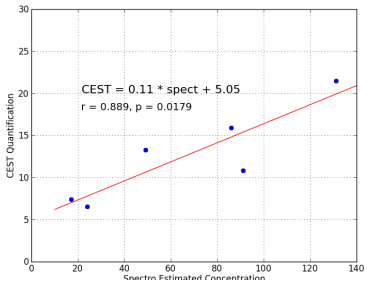

Fig. 3. *GlycoCEST and 1H-MRS compared. The glycoCEST water attenuations were correlated with the 1H-MRS derived estimates of glycogen concentrations.*

References:

1. Ouwerkerk R, Pettigrew RI, Gharib AM. Radiology 2012;265(2):565-575.
2. Kim M, Gillen J, Landman BA, Zhou J, van Zijl PC. \Magn Reson Med 2009;61(6):1441-1450.
3. Nilsson LH, Hultman E. Scand J Clin Lab Invest 1974;33(1):5-10.
4. Rothman DL, Magnusson I, Katz LD, Shulman RG, Shulman GI. Science 1991;254(5031):573-576.
5. van Zijl PC, Jones CK, Ren J, Malloy CR, Sherry AD. Proc Natl Acad Sci U S A 2007;104(11):4359-4364.
6. Bottomley PA. Spatial localization in NMR spectroscopy in vivo. Ann N Y Acad Sci 1987;508:333-348.
7. Vanhamme L, van den Boogaart A, Van Huffel S. I. J Magn Reson 1997;129(1):35-43.

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