Empirical Modeling of B_1 Inhomogeneity Correction for Absolute Quantitation of Hepatic Glycogen Using Non-localized ^{13}C MRS

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Purpose: ^{13}C surface coil based measurement of hepatic glycogen is useful for studying hepatic metabolism and its modulation by treatment. Surface coils provide an inherent spatial localization and a high sensitivity to tissues close to the coil due to their inhomogeneous B_1 field. The B_1 field drops off with increased distance from the coil. When ^{13}C surface coils are used for measuring the hepatic glycogen content, an elementary volume in the liver which is closer to the coil has a higher contribution to the total voltage induced in the surface coil than a volume which is farther away, due to the B_1 inhomogeneity. In practice, this means that differences in the thickness of the subcutaneous fat can confound inter-subject glycogen comparisons in the absence of any B_1 correction. For ^{13}C coils, B_1 correction has been performed in the past by first calculating the B_1 field distribution based on analytical model of magnetic field for the ^{13}C coil geometry, registering this information onto a proton image, and then integrating the B_1 field over the sensitive volume. However performing a three dimensional numerical integration over an ill-defined sensitive volume within the liver is difficult. The current work presents a simpler empirical model for evaluating the B_1 correction factors, based on a series of phantom experiments. The model for a ^{13}C surface coil can be set up prior to the in-vivo studies, and can be readily integrated into the post-processing protocols for absolute quantitation of hepatic glycogen from the non-localized ^{13}C liver spectrum.

Method: Assuming that TR >> T_1, the total voltage induced in the ^{13}C circular surface coil due the total excited volume within the liver, in a non-localized pulse-acquire experiment can be given by [1]:

$$S \propto \iiint M_0 B_1(x,y,z)\sin\left(\gamma B_1(x,y,z)T_p\right)dxdydz \qquad (1)$$

where $B_1(x,y,z)$ is the B_1 field within an elementary liver volume at the spatial location (x,y,z), γ is the ^{13}C gyromagnetic ratio, T_p is the pulse duration, and M_0 is the equilibrium longitudinal magnetization within the elementary volume, which is assumed to be homogeneous over the entire excited liver volume. Due to differences in the subcutaneous fat thickness, B_1 field distribution within the hepatic volume excited by the ^{13}C surface coil can show considerable variation. Eliminating the subject-specific B_1 field dependency requires the glycogen peak areas to be normalized by a B_1 field inhomogeneity correction factor, G, which can be given by:

$$G = \iiint B_1(x,y,z)\sin\left(\gamma B_1(x,y,z)T_p\right)dxdydz \qquad (2)$$

The above correction factor is a function of the B_1 field within the integration volume and the spatial boundary limits of this volume. Assume that the B_1 field inhomogeneity is largely determined by the coil-geometry rather than the sample conductivity effects and that the volume of integration within the liver is kept constant across different subjects. Under these conditions, location of the integration volume relative to the coil determines the net effect of the B_1 inhomogeneity, and the correction factor reduces to a function of the axial distance between the coil-center and the liver surface. Due the absence of an internal concentration reference in the ^{13}C hepatic spectrum, the absolute quantitation of the hepatic glycogen content in molar units requires the comparison of the in-vivo spectra with that obtained from a glycogen phantom with a known concentration. The coil-loading differences between the in-vivo scans and the phantom acquisition can be compensated by affixing a small acetone reference phantom to the coil, and keeping its position fixed for all scans. The acetone singlet at 210 ppm lies in a region free from any peaks arising from metabolites in the liver or the subcutaneous fat. Taking both the coil-loading and B_1 field inhomogeneity corrections into account, the absolute concentration of the hepatic glycogen can be estimated by [2]:

$$Gly_{in} = \frac{A_{in}^{gly}/A_{in}^{ref}}{G_{corr}(d_{in})} \times \frac{G_{corr}(d_{phan})}{A_{phan}^{gly}/A_{phan}^{ref}} \times Gly_{phan} \qquad (3)$$

where A_{in}^{gly} and A_{phan}^{gly} are the glycogen C1 peak areas in the in-vivo spectrum and the glycogen phantom spectrum, A_{in}^{ref} and A_{phan}^{ref} are the acetone peak areas in the in-vivo spectrum and the glycogen phantom spectrum, Gly_{in} and Gly_{phan} are the in vivo and phantom glycogen concentration in molar units, d_{phan} is the coil-glycogen phantom distance, and d_{in} is the coil-liver distance. From Eq. 3, it is evident that the need for explicitly modeling $G_{corr}(d)$ can be avoided if the $d_{phan} = d_{in}$. However this requires a separate phantom scan to be repeated for every possible in-vivo coil-liver distance.

If the A_{phan}^{gly} and A_{phan}^{ref} values measured from a limited set of coil-phantom distances are available, the $A_{phan}^{gly}/A_{phan}^{ref}$ ratio at arbitrary distances from the coil can be obtained by polynomial interpolation. Let r_i represent the normalized glycogen phantom peak area, $A_{phan}^{gly}/A_{phan}^{ref}$, measured at a coil to glycogen phantom of d_i. Consider a scatter plot of (r_i, d_i) duplets obtained by repeating the phantom scan for a range of d_i values, reflecting the expected range of in-vivo coil-liver distances. Let $R(d)$ be a n^{th} order polynomial in d, which best fits the (r_i, d_i) points in the least squares sense. The polynomial, $R(d)$ can be used obtain the $A_{phan}^{gly}/A_{phan}^{ref}$ value at arbitrary coil-liver distances, and can be incorporated in Eq. (3):

$$Gly_{in} = \frac{A_{in}^{gly}/A_{in}^{ref}}{G_{corr}(d_{in})} \times \frac{G_{corr}(d_{in})}{R(d_{in})} \times Gly_{phan} = \frac{A_{in}^{gly}/A_{in}^{ref}}{R(d_{in})} \times Gly_{phan} \qquad (4)$$

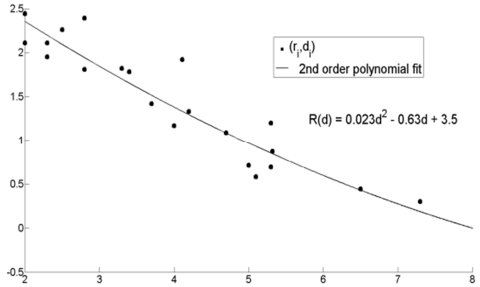

Fig. 1 – r_i vs. d_i

Results: ^{13}C pulse-acquire experiments were performed on a 100 mM glycogen phantom, with different coil-phantom distances. The scatter plot of the $A_{phan}^{gly}/A_{phan}^{ref}$ values as a function of distance, and a 2nd order polynomial fit are shown in Fig. 1. A 2nd order model was chosen to avoid inflection points and to ensure that the model is strictly decreasing with distance. No additional B_1 field-mapping scans are needed during the in-vivo scans. Eq. (4) was used to calculate the absolute glycogen concentration in 4 healthy subjects, after an overnight fast. The ^{13}C pulse-acquire experiment (TR = 400ms, Pulse duration =0.16ms, Avg = 4096) in free-breathing mode using a dual tuned ^1H-^{13}C flexible surface coil (^{13}C circular coil radius = 5.5 cm). The d_{in} values were measured from the tri-plane localizer image obtained from the ^1H element of the coil. The absolute glycogen concentrations measured using Eq. (4) are shown in Table 1. The mean glycogen concentration for the 4 healthy volunteers was 192.2 ± 23.4 mM. The observed values were close to glycogen concentration of 207.1± 22mM which has been reported in literature for healthy subjects after an overnight fast [3].

Subject ID	Coil-liver distance (cm)	Glycogen (mM)
1	4.2	196.6
2	3.4	168.2
3	3.2	181.5
4	4.4	222.8

Table 1- Glycogen Concentration

References: [1] Evelhoch JL, Crowley MG, Ackerman JJH, JMR 56, 110-124 (1984) **[2]** Slotboom J, Fluck C, Kreis R, Jung B, Nuoffer JM, Boesch C, Proc Intl Soc Magn Reson Med 6:1860 (1998) **[3]** Taylor R, Magnusson I, Rothman DL, Cline GW, Caumo A, Cobelli C, and Shulman GI, J. Clin. Invest. 97, 126-132 (1996).