COMPREHENSIVE SPECTROSCOPIC INVESTIGATION OF LIVER METABOLISM – A FEASIBILITY STUDY

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AUDIENCE: clinically oriented MR spectroscopists **PURPOSE:** Magnetic resonance spectroscopy (MRS) is particularly well suited for the non-invasive assessment of liver metabolism and thus could complement liver biopsies that are indicated only in a few severe clinical situations. While ^{1}H-MRS allows the observation of intrahepatic lipids (IHCL), ^{13}C-MRS can follow glycogen, and ^{31}P-MRS is able to monitor phosphorous metabolites involved in energy supply (phosphomonoester PME, inorganic phosphate Pi, adenosine triphosphate ATP) and reaction constants (k_{AB}), e.g. of the chemical exchange between γ-ATP (= B) and P_i (= A). A combination would give a comprehensive insight into metabolic pathways of carbohydrates and lipids in the liver, which then could be used to characterize liver pathology. One major problem of such an integrated examination, however, is the time to acquire the different nuclei sequentially. Therefore, it would be advantageous to use triple-resonant coils, which allow an examination without repositioning and even by interleaved acquisition of the different nuclei (not yet available in the scanner used in this study). This study evaluates the feasibility of an acquisition scheme with a triple tuned ^{1}H/^{13}C/^{31}P-MRS surface coil using an optimized protocol.

METHODS: Subjects: 6 young, normal-weight, male volunteers (26 ± 3y, BMI: 22 ± 1 kg·m^{-2}) participated in this cross-over, double-blinded study. **Design:** On each of the two visits, subjects were examined on a 3T MR-system (VERIO, Siemens, Erlangen Germany) after an overnight fast and re-examined with an identical protocol 3h after intake of 1.2L carbohydrate solution in portions of 200 mL over a period of 3h. The carbohydrates were given analogous to Décombaz et al (1) and consisted of either fructose (90g with 180g of maltodextrin) or glucose (90g with 180g of maltodextrin).

MR-protocol: A triple tuned, linear polarized ^{1}H/^{13}C/^{31}P-MRS surface coil (RAPID Biomedical, Rimpar Germany; ^{1}H-butterfly 24cmx18cm, ^{13}C-loop 10cm, ^{31}P-loop 12cm) allowed an observation of all nuclei with a single, image-guided positioning. A chromium-doped acetone solution of phenylphosphonic acid on the outer side of the surface coil served as external reference. A work-in-progress shimming package (Siemens, Erlangen Germany) allowed the acquisition of homogeneity data in one breath-hold for all nuclei, followed by post-hoc calculation of the shim currents for any selected region. **^{1}H-MRS:** 3 non-water-suppressed and 3 water-suppressed PRESS-localized spectra during breath-hold (TR 1.8s, TE 30ms, 8 acquisitions, typical size RLxAPxHF 25x15x30mm^3) were separately averaged. **^{13}C-MRS:** Acquisition (TR 200ms, 4096 averages, total 14min) with adiabatic excitation pulses (glycogen on the center-frequency), and 2 spatial saturation bands on abdominal muscle (at center frequency to avoid chemical shift artifacts for glycogen). CW-decoupling (50% of acquisition, 100 Hz downfield of water) was monitored by the decoupling of the C=C lipid resonances. **^{31}P-MRS**: Saturation transfer of the γATP-resonance to the Pi resonance or control saturation at the mirror frequency was done according to Buehler et al. (2) in an interleaved series of 4 acquisitions each (TR 2s, saturation 1.4s, 64 averages for each series, total 17min). Under constant saturation of the γ-ATP resonance, an inversion recovery experiment with adiabatic pulses determined T1* (8 inversion times, TR 3s, averages 32 each, total 13min). The concentration of phosphate metabolites was determined from an average of 2-3 relaxed spectra (TR 10s, 16 averages each). Reference signals from phenylphosphonic acid (^{31}P) and acetone (^{13}C) were acquired with the center frequency shifted to the respective resonance line.

RESULTS: Using a small phantom in the coil center, the 180 degree pulses for ^{13}C- and ^{31}P (500us) of the triple tuned coil (typical double-tuned coils in brackets) were 98V (60V) and 105V (80V), respectively. Variations of the reference signals within subjects were negligible. As seen in the Figure, IHCL shows large inter-individual variations without any consistent trend due to the intake of carbohydrates. Glycogen increased with fructose, however, without reaching significance, and stayed almost constant with glucose. PME and Pi increased after the intake of carbohydrates, however, only the intake of glucose reached significance ($p<0.01$ for both). ATP and the reaction constant k_{AB} were reduced after intake of either carbohydrate, both observations without reaching significance. The complete examination could be reduced to about 1.5h with increasing experience of the operator.

DISCUSSION: Within a tolerable examination time, it is feasible to obtain ^{1}H-images, ^{1}H-spectra of lipid content, ^{13}C-spectra of glycogen, ^{31}P-spectra of phosphorous metabolites and reaction constants, using a triple tuned surface coil at 3 Tesla without any repositioning of the subject. Since the number of subjects was limited in this feasibility study, the results did not yet reach statistical significance. However, the observed trends point towards meaningful and hypothesized findings: glycogen increases after intake of fructose more than after intake of glucose (1), lipid metabolism is not affected at this time scale, phosphorylated sugar results in an increase of PME, P_i is increased, while ATP is reduced (3).

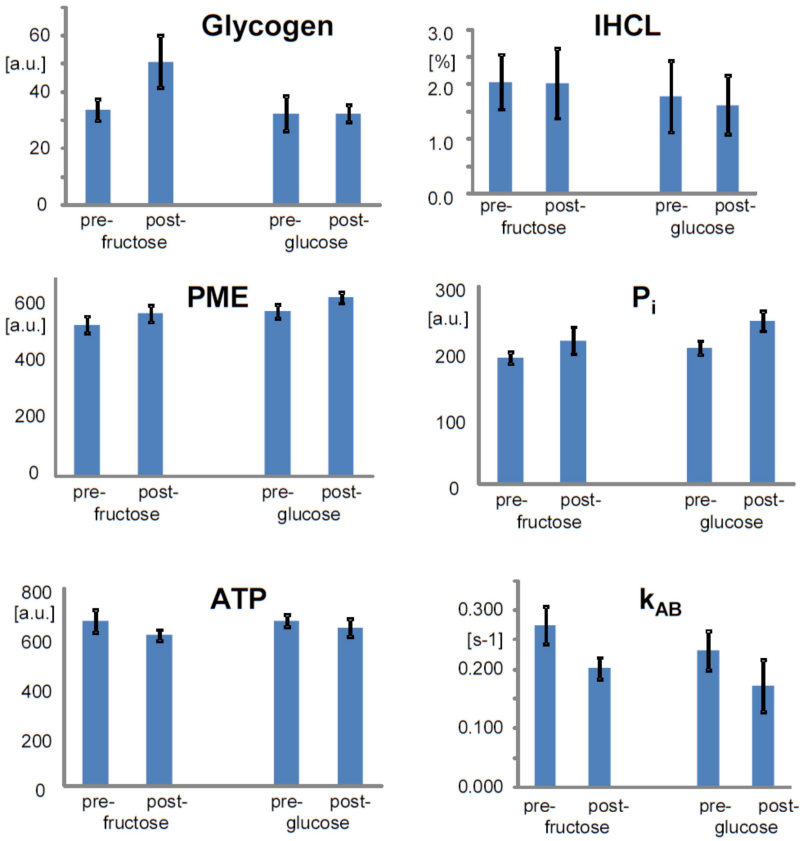

Figure: Metabolite levels and k_{AB} (mean±1sem) pre- and post-intervention

REFERENCES: (1) Decombaz et al. Med Sci Sports Exerc 43:1964 (2011). (2) Buehler et al. Proc.ISMRM 19:3005 (2011). (3) Boesch et al. Magn Reson Imaging 15:1067 (1997).

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