Combination of pre-suppression of lipids and MEGA-sLASER for the detection of BHB in the human liver

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Introduction: The ketone body beta-hydroxybutyrate (BHB, 3-hydroxybutyrate) is produced by the liver and functions as an alternative substrate for metabolism during fasting[1]. There are indications from animal studies that ketogenesis can modulate liver fat[2]. Non-invasive detection of BHB in the liver will give insight into the relevance of this pathway in humans. Subtraction-based spectral editing techniques have been used to detect the BHB in the human brain[3], but detection in the liver is challenging, as respiratory motion will result in incomplete suppression of the (large) overlapping lipid signal at 1.3 ppm. To efficiently suppress this hindering signal, single shot, multiple quantum coherence (MQC) sequences[4] can be used, which however lead to an intrinsic 50% signal reduction when compared to a subtraction-based technique. Here we hypothesize that (partial) pre-suppression of the large lipid CH_2-signal with the use of an additional inversion pulse before a MEGA-sLASER sequence, will provide accurate and robust detection of BHB irrespective of respiratory motion, with higher signal yield when compared to MQC.

Materials and Methods: Experiments were performed on a 3T MR system (Achieva 3T-X Philips Healthcare, Best, Netherlands) using a 32-channel sense cardiac/torso coil (Philips Healthcare, Best, Netherlands). A phantom containing 20% intralipid, BHB, lactate and creatine (each 10 Mm) was used for all experiments. A MEGA-sLASER sequence was used for the detection of BHB, once with, and once without inversion pulse for pre-suppression of lipids, with the following parameters: TR/TE=3000/20 ms, NSA=16, Voxel=30X30X30 mm, datapoints=2048, target frequency at 4.1 & 5.3 ppm for MEGA pulses (Sinc-Gaussian pulse, bandwidth 200 Hz). A hyperbolic secant pulse (bandwdith 1300 Hz) was used for inversion prior to the MEGA-sLASER (TI = 200 ms). In addition, we acquired spectra with series of TIs (50, 100, 200, 300, 400, 500, 750, 850, 1000 and 1200 ms) to calculate the T_1 of BHB in our designed phantom. All spectra were post-processed with a home written MATLAB script.

Results: The spectra acquired from the phantom are depicted in figure 1. The signal intensity of BHB with the TI-MEGA-sLASER (Fig1D) was 75% when compared to the MEGA-sLASER (Fig1B). The T_1 of BHB was found to be approximately 1080 ms in our phantom.

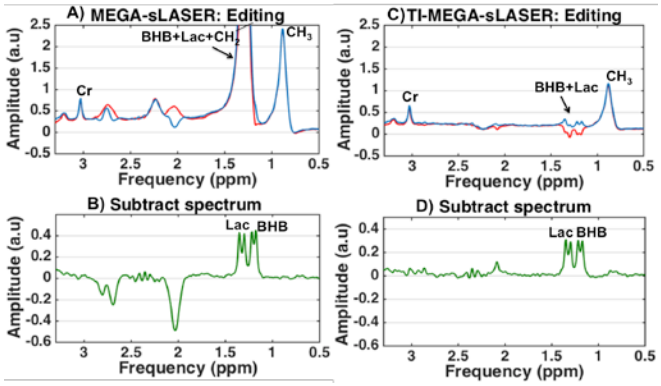

Fig1: Spectra acquired with MEGA-sLASER (A) and TI-MEGA-sLASER (C) with MEGA pulse frequency of 4.1 (blue) and 5.3 ppm (red) respectively. The subtraction spectra obtained with MEGA-sLASER and TI-MEGA-sLASER are shown in panel B and D respectively.

Discussion: The insertion of the inversion pulse leads to pre-suppression of the large methylene signal at 1.3 ppm. Although suppression of the lipid signal in the phantom was successful with MEGA-sLASER only, the inversion pulse will be necessary *in vivo* to get maximal suppression of the lipid signal. As expected, the inversion pulse only leads to a modest signal loss of BHB signal due to long T_1 of the BHB. The signal yield *in vivo* will be different due to a difference T_1 of BHB in the liver. This will be evaluated in future studies.

Conclusion: Our proposed TI-MEGA-sLASER sequence leads to a higher signal yield when compared to MQC and can thus be used as an alternative editing sequence to detect BHB in the human liver.

References: 1.Robinson A.M et al., Physiol. Rev.(1980), 2. Cotter David G et al., J.Clin.Invest. (2014), 3. Pan Jullie W et al., J Cereb Blood Flow Metab (2002), 4. He Q et al., J. Magn. Reson B (1995).

Acknowledgements: This work was conducted within the Health-Holland framework and financially supported by Unilever Research Vlaardingen and Health-Holland.