On the Evaluation of 31P MRS Human Liver Protocols.

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Introduction: ^{31}P MRS of the human liver has been proposed as a tool for non-invasive determination of liver fibrosis. There are mainly six resonances of interest in ^{31}P MRS of the human liver: PME (phosphomonoester), Pi (inorganic phosphate), PDE (phosphodiester) and γ-, α-, β-ATP (adenosine triphosphate, or more strictly NTP). The resonances of interest for staging of liver fibrosis are mainly PDE and PME described by the ratio known as the 'anabolic charge', AC (=[PME]/([PME]+[PDE])) which has been shown to correlate with liver fibrosis [Norén *et al* 2008]. A major problem in the usage of ^{31}P MRS is the low sensitivity leading to long scan times which may results in motion-induced artifacts due to lack of patient compliance. Several methods have the potential for improving the accuracy and sensitivity of ^{31}P MRS in particular of PDE and PME. Proton decoupling improves the spectral resolution in particular in the PME and PDE regions, and also allows the separation of the MP (Membrane Phosphates at c. 0 ppm, referenced to PCr at -2.35 ppm) resonance from PDE. In addition, the Nuclear Overhauser enhancement (NOE) potentially increases the SNR of the metabolites. This study aimed at finding an optimal protocol for ^{31}P MRS in the human liver using a clinical scanner, within a clinically acceptable scan time of 15-20 minutes with respect to the following three parameters (1.) Proton decoupling, (2.) NOE enhancement, (3.) Repetition time. Finally, the standard deviations of AC, AC including MP and PME/PDE of the choosen protocol was determined in a group of healthy volunteers.

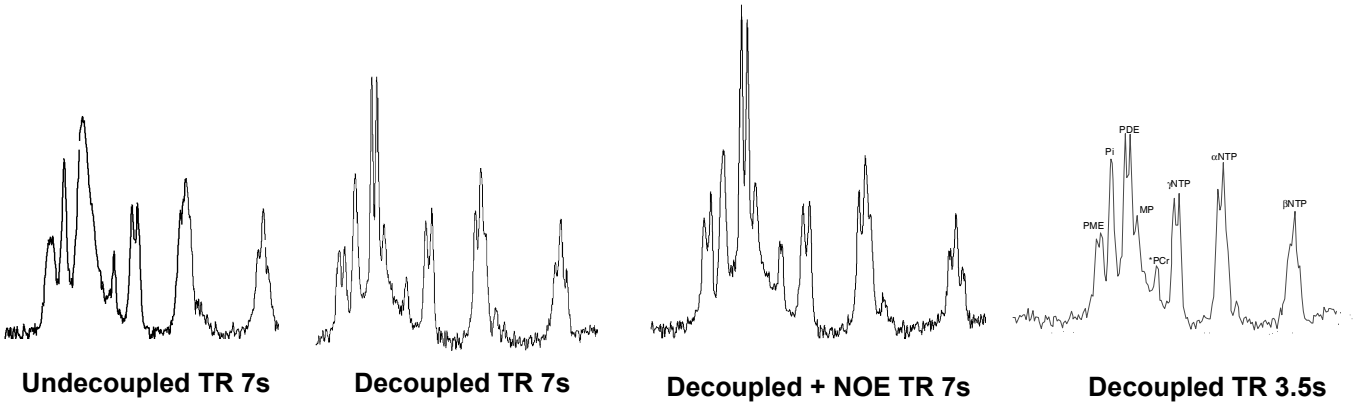
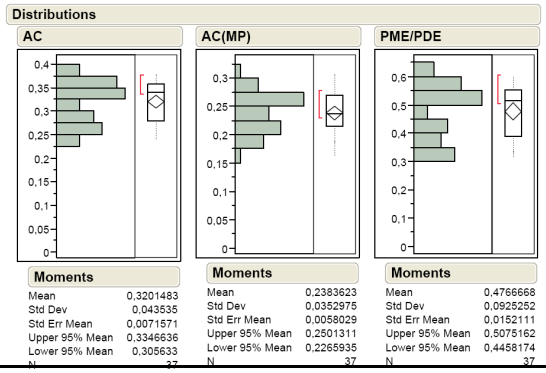


***Fig**. The ^{31}P MRS liver spectra of healthy volunteers (from left n/m = 16/4; 16/4; 8/4; 8/4). Assignments of the major resonances includes the PCr artifact labeled *.*

Materials and Methods: The data acquisition was divided into two parts. In the FIRST PART four healthy volunteers were examined, each individual was investigated in four sessions, and these sessions consisted of four different protocols (except one of the sessions) in a randomized order. Every session included; a non-decoupled, as well as a decoupled ^{31}P MRS using a TR of 7 s. One session per individual had an extra decoupled ^{31}P MRS acquired using a TR of 7 s. Furthermore, each individual was examined using two of the following signal acquisition methods; decoupled ^{31}P MRS with a shorter (3.5 s) and a longer (10 s) TR. In addition, a decoupled ^{31}P MRS utilizing NOE enhancement with a TR of 7 s was acquired. In the SECOND PART, the selected optimized protocol was used to examine 13 healthy volunteers once.

A 1.5 T MR-scanner (Philips Medical systems, Best, the Netherlands) was used together with a 10 cm circular ^{31}P receive/transmit RF-coil. For localizer images, as well as for the proton decoupling, the built-in body coil was used. In PART 1 the sequence parameters used were (unless otherwise stated) TR/averages/pulse sequence/ = 7s/192/ISIS using proton broadband decoupling, but no NOE. In PART 2, the protocol was shortened to 128 averages. The subjects were placed in supine position and all spectra were acquired during free breathing. The MRS voxel (6x6x6 cm^3) was placed in liver tissue as close to the coil as possible.



TR = 7s	AC	AC (MP)	PME/PDE
Non-decoupled (n=16)	0.30±0.04	0.24±0.03	0.42±0.08
Decoupled (n=20)	0.32±0.05	0.24±0.04	0.47±0.10
Decoupled+NOE (n=8)	0.32±0.04	0.24±0.02	0.48±0.09

jMRUI, MRUI for Java (Magnetic Resonance User Interface, MRUI, EC Human Capital and Mobility Networks, France) [1] was used for processing of ^{31}P MRS using the AMARES algorithm with prior knowledge [2] for quantification of the resonances.

Results: The amplitudes where analysed using a 3-factorial ANOVA model. The measurements in part one are shown in the Table. Using a shorter TR (3.5 s) resulted no significant difference on the AC(incl. MP) value (+0.01±0.008, p<0.25), although it yielded a larger value of AC w/o MP (+0.026±0.01, p<0.033). However, there was a strong saturation effect on both PDE and PME when a TR of 3.5 s was used (see Fig.). $T1_{PME}$ was fitted to 2.3 s, $T1_{PDE(excl.\ MP)}$ to 3.6 s., and $T1_{MP}$ was fitted to 1.1 s. The longer TR (10 s) did not result in any significantly different values than by using TR of 7 s, p<0.05. Thus the results showed no significant difference between the ratios using the different protocols at a TR of 7 s (see the table), p<0.05, in the Figure summed spectra from all ^{31}P spectra are shown. The metabolite ratios collected using decoupling and a TR of 7 s are shown in the histogram, in which data from both parts of the study are presented.

Discussion: Estimates of AC(incl MP) were comparable independent of the use of proton decoupling, NOE enhancement and different TR. We believe that this is an outcome caused by the differences in T1 between PDE and MP (T1 of PDE is longer compared to T1 of PME.) MP is probably not linked to the altered metabolism during fibrosis development, and therefore it may be an advantage to use proton decoupling as it enables efficient separation of MP from PDE. By inducing NOE, the SNR of the PME and PDE metabolite signals improved. However, we opted for not including NOE in the optimized protocol as we are uncertain on the inter-subject stability of this enhancement. Finally, we suggest that a TR of 7 s is both sufficiently long to limit the risk of T1-smearing associated with ISIS volume selection. It is also long enough to limit the potentially strong saturation effects caused by the long T1 of PDE and PME.

References: ***[1]**Naressi A, Couturier C, Devos JM, et al. Java-based graphical user interface for the MRUI quantification package. MAGMA 2001;12:141-52. **[2]** Vanhamme L, van den Boogaart A, Van Huffel S. J Magn Reson 1997;129:35-43**; **[3]** Noren B, Dahlqvist O, Lundberg P, et al. Eur J Radiol. 2008 May;66(2):313-20.*