# Reproducibility evaluation of liver metabolite parameters: $^{1}$H decoupled - $^{31}$P MRSI of normal volunteers at 1.5T

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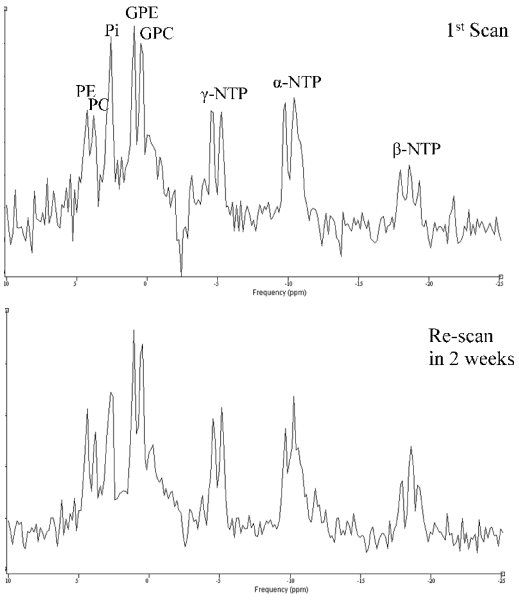
**Objective:** *in vivo* $^{31}$P MRS is a promising tool for evaluation of various liver diseases noninvasively, but reproducibility and consistency of metabolite parameters is a common concern in studies [1,2]. The purpose of this study is to evaluate the reproducibility of liver $^{31}$P metabolites measured by $^{1}$H decoupled - $^{31}$P MRSI at 1.5T.

**Methods:** Experiments were performed on a G.E. 1.5 T scanner equipped with a $^{1}$H decoupler. 13 healthy adults were scanned twice with a 2 or 3 week interval between studies. Subjects fasted for at least 3 hours prior to scanning. A dual $^{1}$H/$^{31}$P coil was positioned adjacent to the liver. Following imaging, $^{1}$H decoupled - $^{31}$P 3D MRSI was performed using a pulse-and-acquire sequence with a flip angle of 45° in the liver area of interest and Waltz - 4 decoupling. Voxel sizes ranged from 42 to 63 cm$^3$. Spatial Fourier transform was performed using SAGE/IDL (GE) or 3DiCSI (Columbia University). Voxel shifting was performed to obtain single spectra from voxel locations as close to identical as possible. Spectra were fit in the time domain using MRUI [3]. Peak areas were corrected for flip angle/saturation and coil reception profile and normalized with respect to a TPP standard [4]. There were no corrections for point-spread function and NOE. Normalized quantities were reported for phosphoethanolamine (PE), phosphocholine (PC), inorganic phosphate (Pi), glycerophosphoethanolamine (GPE), glycerophosphocholine (GPC), and nucleoside triphosphates (NTP). Phosphomonoester (PME) was calculated as the sum of the areas of the PE and PC peaks, and phosphodiester (PDE) as the sum of GPE and GPC. The pH was measured based on the chemical shift difference between Pi and α-NTP. Coefficients of variation were calculated to assess inter- and intra- subject reproducibility.

**Results:** Examples of liver $^{31}$P MR spectra from one subject's 1$^{st}$ scan and re-scan are shown in the figure. PE, PC, GPE and GPC peaks were well resolved. The spectra appeared qualitatively similar in the repeated scan. Metabolite concentrations (normalized units, n.u.) and inter-/intra-subject coefficient of variations (CV) for all subjects are listed in Table 1. It should be noted that normalized values cannot be compared to literature values due to differences in technique. The PH value had superb consistency with intra-and inter- subject variation less than 1%. Inter- and intra-subject CV ranged from 11% to 25% for all normalized concentrations. Overall, inter-subject reproducibility was similar to intra-subject reproducibility with average CV of 16% and 18% respectively. We would assume that intra-subject reproducibility reflects the inherent signal-to-noise limitations of the technique as well as any errors in the correction for flip angle and B1 sensitivity over the voxel of interest. Inter-subject variability reflects the above parameters as well as possible biological differences in liver metabolism between subjects. The similarity between inter- and intra- subject variability suggests that biological differences in liver $^{31}$P metabolism in healthy control subjects are not large enough to exceed uncertainties produced by signal-to-noise limitations and possible errors in the flip angle and saturation correction factors.




**Conclusion**: The coefficients of variation in liver $^{31}$P metabolites at 1.5T range from 11% to 25%, and intra-subject reproducibility did not exceed inter-subject reproducibility. Changes in $^{31}$P metabolites due to biological alterations in the liver would probably need to reach 25% to be detected with significance at 1.5T. Higher field strength is needed to improve precision.

**References:** 1. Solga SF, et al. Liver International 2005; 25: 490-500. 2. Sijens PE, et al. MRI 1998; 16: 205-211. 3. Vanhamme L, et al. J Magn Reson 1997; 129: 35-43. 4. Zakian KL,et al. Magn Reson Med 2005; 54: 264-71

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Table1: Liver metabolite concentrations (n.u.) and inter-/intra- subject coefficients of variation (CV) in 13 normal volunteers.

| | PE | PC | PME | Pi | GPE | GPC | PDE | β-NTP | PH |
|---|---|---|---|---|---|---|---|---|---|
| 1$^{st}$ Scan (mean±SD) | 2.71±0.69 | 2.99±0.59 | 5.44±0.97 | 5.23±0.75 | 10.56±2.41 | 14.29±5.15 | 24.75±6.81 | 2.61±0.55 | 7.39±0.06 |
| Re-scan (mean±SD) | 2.76±0.77 | 3.02±0.53 | 5.77±1.14 | 4.91±0.93 | 9.81±2.15 | 13.73±3.84 | 24.34±5.48 | 2.62±0.56 | 7.40±0.05 |
| Inter-subject CV | 0.13 | 0.11 | NA* | 0.11 | 0.16 | 0.25 | 0.20 | NA* | 0.004 |
| Intra-subject CV | 0.24 | 0.16 | 0.19 | 0.12 | 0.14 | 0.20 | 0.15 | 0.21 | 0.006 |

* The inter-subject CV for PME and β-NTP are less meaningful because the correlation coefficients are slightly negative (-0.009 and -0.26).