Analysis Report

Bruker IVDr Quantification in Plasma/Serum B.I.Quant-PS™

Sample ID:	HB-COVID0001_expno10.100000.14r
Measuring Date:	01-Jul-2020 14:55:49
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Quantification Method Version:	Quant-PS 2.0.0

Disclaimer

RESEARCH USE ONLY: This is no clinical diagnostic analysis report. Must not be used for clinical (medical or IVD) diagnosis or for patient management! Additional concentration range information (95% range) provided numerically or graphically in this report must not be used for clinical diagnostic interpretation.

Application of B.I.QuantPS 2.0 requires use of Bruker's B.I.Methods SOP for plasma and serum.

Summary

The spectroscopic fingerprint of the sample is consistent with a serum or a heparin plasma profile. The following metabolites were found with concentrations outside the 95% range of Bruker Quant-PS 2.0.0 plasma/serum metabolite concentration data base:

Amino acids and derivatives: Creatine (0.10 mmol/L), Creatinine (0.18 mmol/L), Isoleucine (0.13 mmol/L), Leucine (0.34 mmol/L), Phenylalanine (0.17 mmol/L), Valine (0.52 mmol/L),
Carboxylic acids: 2-Hydroxybutyric acid (0.20 mmol/L), Formic acid (0.04 mmol/L), Succinic acid (0.07 mmol/L),
Keto acids and derivatives: 3-Hydroxybutyric acid (1.57 mmol/L), Acetoacetic acid (0.55 mmol/L), Acetone (0.42 mmol/L),
Sugars and derivatives: Glucose (17.05 mmol/L).

Further detailed information is provided on the following pages.

Contents

1 Alcohols and derivatives

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
Ethanol	< 0.10	0.10	0.000	0 ○	3.380	⩽ 0.82	

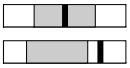
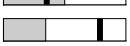
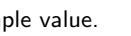
(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

2 Amines and derivatives

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
Trimethylamine-N-oxide	< 0.08	0.08	0.025	99 ●	0.086	⩽ 0.08	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

3 Amino acids and derivatives

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
2-Aminobutyric acid	0.06	0.05	0.062	1 ○	0.226	⩽ 0.10	
Alanine	0.36	0.02	0.357	100 ●	0.007	0.29 - 0.64	
Asparagine	< 0.05	0.05	0.000	0 ○	4.416	⩽ 0.08	
Creatine	0.10	0.01	0.098	100 ●	0.003	⩽ 0.07	
Creatinine	0.18	0.01	0.181	100 ●	0.003	0.06 - 0.14	
Glutamic acid	0.18	0.05	0.175	92 ○	0.021	⩽ 0.24	
Glutamine	0.67	0.02	0.665	99 ●	0.021	0.30 - 0.83	
Glycine	0.25	0.01	0.245	98 ●	0.014	0.17 - 0.44	
Histidine	0.12	0.02	0.117	99 ●	0.003	0.07 - 0.16	
Isoleucine	0.13	0.03	0.130	99 ●	0.011	0.03 - 0.11	
Leucine	0.34	0.01	0.341	99 ●	0.015	0.07 - 0.20	
Lysine	0.15	0.04	0.155	52 ○	0.153	⩽ 0.29	
Methionine	0.06	0.05	0.057	82 ○	0.010	0.05 - 0.13	
N,N-Dimethylglycine	< 0.01	0.01	0.006	99 ●	0.000	⩽ 0.01	
Ornithine	0.11	0.02	0.113	13 ○	0.101	⩽ 0.16	
Phenylalanine	0.17	0.03	0.168	99 ●	0.005	⩽ 0.07	
Proline	< 0.05	0.05	0.000	0 ○	3.017	⩽ 0.59	
Sarcosine	< 0.01	0.01	0.003	55 ○	0.001	⩽ 0.01	
Threonine	0.16	0.04	0.160	67 ○	0.110	⩽ 0.24	
Tyrosine	0.05	0.03	0.049	99 ●	0.003	⩽ 0.08	
Valine	0.52	0.03	0.523	100 ●	0.007	0.15 - 0.35	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

4 Carboxylic acids

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
2-Hydroxybutyric acid	0.20	0.15	0.200	66 ○	0.121	⩽ 0.17	
Acetic acid	0.04	0.01	0.040	100 ●	0.001	⩽ 0.06	
Citric acid	0.20	0.03	0.197	88 ○	0.061	⩽ 0.21	
Formic acid	0.04	0.02	0.039	99 ●	0.001	⩽ 0.03	
Lactic acid	3.4	0.03	3.400	100 ●	0.086	2.23 - 7.14	
Succinic acid	0.07	0.01	0.071	100 ●	0.001	⩽ 0.01	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

5 Essential nutrient

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
Choline	< 0.05	0.05	0.010	77 ○	0.002	⩽ 0.06	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

6 Keto acids and derivatives

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
2-Oxoglutaric acid	< 0.02	0.02	0.007	21 ○	0.011	⩽ 0.02	
3-Hydroxybutyric acid	1.6	0.02	1.566	100 ●	0.013	⩽ 0.26	
Acetoacetic acid	0.55	0.01	0.552	97 ●	0.014	⩽ 0.02	
Acetone	0.42	0.01	0.418	99 ●	0.014	⩽ 0.06	
Pyruvic acid	0.04	0.03	0.039	97 ●	0.002	⩽ 0.07	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

7 Sugars and derivatives

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
D-Galactose	< 0.11	0.11	0.000	0 ○	1.886	⩽ 0.11	
Glucose	17	0.54	17.047	100 ●	0.058	1.73 - 6.08	
Glycerol	0.35	0.08	0.350	13 ○	0.461	⩽ 0.44	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

8 Sulfones

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
Dimethylsulfone	0.01	0.01	0.011	97 ●	0.000	$\leqslant$ 0.02	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

9 Technical additives

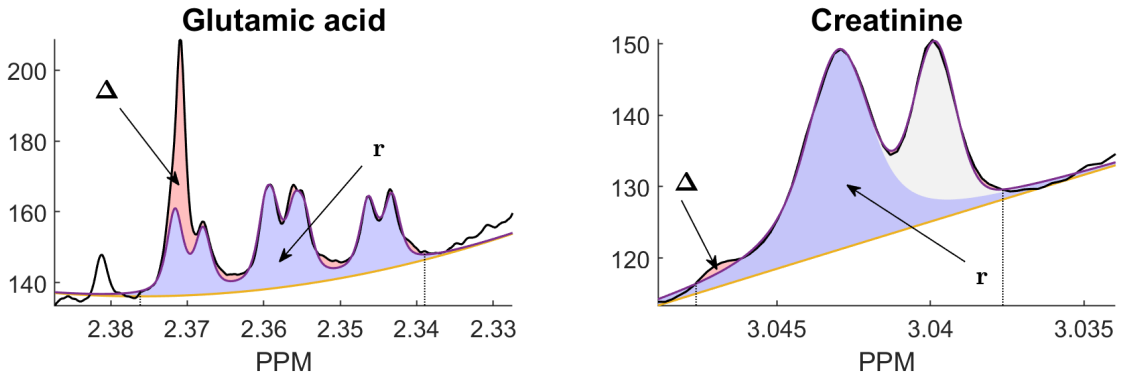
Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range mmol/L	Graphics (*)
Ca-EDTA	$<$ 0.50	0.50	0.004	0 ○	0.004	$\leqslant$ 0.50	
K-EDTA	$<$ 0.50	0.50	0.037	98 ●	0.003	$\leqslant$ 0.50	

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

10 Explanations

This section contains the definition of the parameters used above. In the section 10.1 a short manual, how to interpret the results, is presented. The section 10.2 contains the exact definitions of the parameters $\mathbf{r}$, ρ and $\mathbf{\Delta}$.

10.1 How to read the result



(a) Single signal fitting.

(b) Simultaneous fitting of two signals.

Figure 1: Examples of fitting.

In the figure 1(a), the black line, the blue line and the yellow line represent the original spectrum, the calculated signal fit and its baseline, respectively.

The blue area relates to the metabolite concentration to be determined and the red area represents a residue.

In case of the signal overlap a different approach is used: two or more overlapping signals are being fitted simultaneously. The most iconic example of such signals are the ones generated by $\mathrm{CH_3}$ groups of Creatinine and Creatine. In such a case, the blue line and the grey area relate the sum of all fitted signals. The blue area corresponds to the concentration of the metabolite of interest (cf. figure 1(b)).

10.1.1 Result parameters

a) **Conc.** is the final result concentration of the metabolite,

b) **LOD** is the *limit of detection* of the given metabolite,

c) $\mathbf{r}$ is the *raw concentration* i.e. the concentration equivalent of the resulting signal fit prior to comparing to **LOD** (relates to the blue area, cf. α)),

d) ρ is the correlation of lineshape metabolite signal with calculated fit characterizing the match between metabolite signal and fit (cf. β)),

e) $\mathbf{\Delta}$ is the concentration equivalent of the difference between metabolite signal and calculated fit (residue corresponding to the the red area, cf. γ)).

10.1.2 Different fit situations

Now we will describe the main fit cases.

i) In an ideal situation, where the fit corresponds fully to a metabolite signal well above **LOD**:
   - the raw concentration is similar to the final result concentration,
   - the correlation is $\geqslant 95\%$ (indicated by ● displayed next to the value, otherwise the mark ○ is being used),
   - the residue **Δ** is close to zero mmol/L.

ii) Similar to situation described in i), but raw concentration below **LOD**. Generally, only an upper limit (e.g. $<$ **LOD**) can be provided. Especially, if the difference between raw concentration $\mathbf{r}$ and the final concentration **Conc.** is small, use the graphical figure displayed when pointing the cursor on the metabolite name for further visual inspection and validation. If a metabolite signal can be clearly discriminated from the rest of the spectrum and the calculated fit represents the respective signal well, the raw concentration may be used as approximative concentration estimate.

iii) Low correlation combined with large residual **Δ**. Such situation may arise in case of significant signal overlap, e.g. if a doublet signal of a metabolite to be quantified is overlaid with a large singlet. Use the graphical figure displayed when pointing the cursor on the metabolite name for further visual inspection and validation. If the non-overlaid part of the signal is well fitted, the final calculated concentration may still be used with confidence depending on the degree and nature of signal overlap.

iv) Combination of ii) and iii). Use the graphical figure displayed when pointing the cursor on the metabolite name for further visual inspection and validation.

10.2 Detailed definitions

Let s, f and b denote the functions describing the *raw spectra*, *fitted curve* and *(fitted) baseline* respectively. These functions are chosen such that $s \approx f + b$. Moreover, let I be a relevant PPM interval and P_N be the proton number for given metabolite/signal.

α) $\mathbf{r}$ (*raw concentration*) is defined as

$$\mathbf{r} = \frac{1}{P_N} \int_{\mathbb{R}} f(\xi)\, \mathrm{d}\xi.$$

β) ρ is the *correlation* of the functions s and $f + b$, i.e.

$$\rho = \max\big(0, \operatorname{corr}\big(\overline{s}, \overline{f+b}\big)\big)\,,$$

where $\overline{s}$, $\overline{f+b}$ are numerical representations of the functions s and $f + b$ on sufficiently fine mesh of the interval I.

γ) **Δ** is the the area between the raw signal s and the fitted data $f+b$ on the interval I expressed in the term of the concentration, i.e.

$$\mathbf{\Delta} = \frac{1}{P_N} \int_I |s(\xi) - f(\xi) - b(\xi)|\, \mathrm{d}\xi.$$