Influence of different TE on reliability of brain metabolites quantification in high field 1H MRS

Veronika Rackayova[1], Cristina Cudalbu[2], Lijing Xin[1], Nicolas Kunz[3], Jana Starcukova[4], Zenon Starcuk, Jr.[4], and Rolf Gruetter[1,2]

[1]*Laboratory of Functional and Metabolic Imaging, Center for Biomedical Imaging, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Vaud, Switzerland,* [2]*Centre d'Imagerie Biomedicale (CIBM), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Vaud, Switzerland,* [3]*Centre d'Imagerie Biomedicale (CIBM-AIT), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Vaud, Switzerland,* [4]*Institute of Scientific Instruments of the Academy of Sciences of the Czech Republic, Brno, Czech Republic*

TARGET AUDIENCE: Researchers involved in the study of brain metabolism by ^{1}H MRS in high field.

PURPOSE: Proton MR spectra are characteristic by metabolites overlapping which complicates the quantification but in the same time by great number of detectable metabolites offering a valuable metabolic information. For the latter we need precise quantification and this is highly influenced by the TE used during the measurement. The advantages of high magnetic field are the increased SNR, better spectral resolution and thus increase in number of reliable quantifiable metabolites. But with increasing magnetic field all metabolites have tendency to shorten their apparent T_2 relaxation time [1,2,3] and thus the use of ultra-short TE (<10ms) is recommended to avoid signal loss due to the transversal relaxation but also J-modulation of coupled metabolites. However, it is not always easy or even feasible to reach ultra-short TE due to technical reasons. Short to moderate TE (10-30ms) still offers the possibility to detect relatively high number of metabolites but for their reliable quantification the corresponding apparent T_2 relaxation has to be taken into an account. The aim of this study was to test how TE affects the SNR, the precision of individual metabolite detection and the number of reliable quantifiable metabolites.

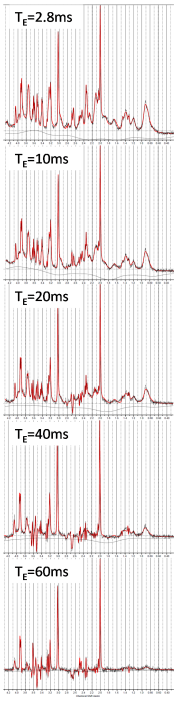

***Fig 1**: Representative spectra for each TE.*

METHODS: Measurements were performed on a 9.4T system (Varian/Magnex Scientific) using 4 healthy male Sprague-Dawley rats, anesthetized with 1.5% of isoflurane during the experiment. To measure ^{1}H MR spectra, we used a home-built 14mm diameter quadrature ^{1}H surface coil as a transceiver and the SPECIAL spectroscopy sequence with 5 different TE (TE=2.8; 10; 20; 40; 60ms, TR=4s, 240 averages) [5], VOI of 3x3x3mm^3 localized mainly in the hippocampus. First and second order shims were adjusted using FASTMAP (water linewidth of 10-11Hz was kept during the whole course of the experiment). Concentrations of metabolites were estimated by LCModel using a basis-set of 19 metabolites (Ala, Asp, PCho, Cr, PCr, GABA, Gln, Glu, GSH, Gly, Ins, Lac, NAA, Tau, Asc, Glc, NAAG, GPC and PE) created by quantum mechanics simulations for each corresponding TE (using an in house matlab routine or NMRSCOPEb) and water used as internal reference. Final concentrations were corrected to previously published T_2 relaxation constant values of individual metabolites [1,2] and the Cramer-Rao lower bounds (CRLB) were used as reliability measure of the metabolite concentration estimates.

RESULTS AND DISCUSSION: With increasing TE, we could observe decreased number of quantifiable metabolites as well as increase in mean CRLBs (mainly for coupled metabolites) together with decreased SNR due to decrease of absolute signal because of transversal relaxation (Table 1). Calculated absolute concentration values, after correction to transversal relaxation, were unaffected for uncoupled high concentrated metabolites (Cr, PCr, NAA) but also coupled high concentrated ones (Tau, Ins), in the whole range of TE. For the other metabolites, we could observe certain variations what was in agreement with increase in CRLB and thus probably due to less precise quantification. At TE=2.8ms, we were able to quantify 11 metabolites with high precision (CRLB<10%) (Cr, PCr, GABA, Glu, Gln, GSH, Ins, Lac, NAA, Tau, tCho) and 5 metabolites with CBLR=10-30% (Ala, Asp, PCho, Gly, NAAG). CRLB were increasing gradually with increasing TE resulting, at TE=60ms, in only 6 metabolites with CRLB<10% (Cr, PCr, Glu, Ins, NAA, Tau) and 7 with CBLR=10-30% (Ala, Asp, Gln, GSH, Gly, Lac, NAAG). Spectral precision, represented by CRLB, was non-affected in the case of high concentrated singlets (NAA, Cr, PCr, tCho) and also Ins with increasing TE. At TE=60ms, metabolites with J-modulation showed increased CRLB by ~100% (Lac) and ~300% (Gln, Glu, Tau). For some coupled low concentrated metabolites quantification was no more possible (PE, GABA), for others CRLB increased by ~100-200% (Ala, Asp, GSH). In the case of Gly we could observe a decrease in CBRL with increasing TE due to J-modulation of Ins sharing the same resonant frequency, as already published [6]. Low concentrated metabolites with J-coupling showed certain limit in TE for being quantifiable with good precision (Gln, Glu, GSH, Tau, GABA until TE=20ms; Lac, PE until TE=40ms).

		TE [ms]:	2.8	10	20	40	60
		average SNR ± SD:	38.5 ± 1.2	41 ± 1.3	37 ± 1.6	36 ± 2	33 ± 1
		Metabolites	average CRLB ± SD:				
non affected CRLB		Cr	3%±1%	4%±1%	5%±1%	4%±1%	5%±1%
		PCr	3%±1%	3%±0%	3%±0%	4%±1%	4%±0%
		Ins	2%±0%	3%±1%	3%±0%	4%±1%	3%±0%
		NAA	1%±0%	1%±0%	1%±0%	1%±0%	1%±0%
		GPC+PCho	6%±1%	6%±1%	6%±1%	4%±0%	3%±0%
acceptable CRLB until TE=60ms	non affected until TE=40ms	Lac	8%±2%	9%±3%	8%±3%	10%±3%	16%±2%
	non affected until TE=20ms	Gln	3%±1%	6%±1%	6%±0%	15%±4%	18%±3%
		Glu	2%±0%	2%±0%	3%±1%	7%±1%	7%±1%
		GSH	8%±1%	5%±1%	8%±1%	10%±1%	11%±1%
		Tau	2%±0%	2%±0%	3%±0%	5%±1%	8%±1%

***Table 1:** Average values for SNR and CRLB in different TE and for different metabolites.*

CONCLUSION: As expected, TE has an important effect on the reliability of metabolites quantification. Ultra-short TE combined with a reliable quantification software is a preferential choice especially if we are interested in a wide range of metabolites. In addition short TE can also provide a good alternative but the reliability of the quantification algorithm has also to be taken into account. It is important to notice that longer TE can be advantageous in some particular cases (as shown in the case of Gly) but in general shorter TE offers better and more precise quantification for almost all brain metabolites.

***References** [1] Xin L et al, NMR Biomed 2008; [2] de Graaf RA et al, Magn Reson Med 2006; [3] Xin L et al, Magn Reson Mater Phy 2013; [4] Michaeli S et al, Magn Reson Med 2002; [5] Mlynárik V et al, Magn Reson Med 2006; [6] Gambarota G et al, Magn Reson Med 2008.* ***Acknowledgements**.Supported by CIBM of the UNIL, UNIGE, HUG, CHUV, EPFL, the Leenaards and Jeantet Foundations. EU: FP7-PEOPLE-2012-ITN project 316679 TRANSACT*