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Evaluating T2* bias impact and correction strategies in quantitative proton density mapping

Evelyne Balteau[1], Tobias Leutritz[2], Nikolaus Weiskopf[2], Enrico Reimer[2], Antoine Lutti[3], Martina F Callaghan[4], Siawoosh Mohammadi[5] and Karsten Tabelow[6]

[1]Cyclotron Research Centre - GIGA-CRC in vivo imaging, University of Liege, Belgium, [2]Department of Neurophysics, Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [3]Laboratoire de Recherche en Neuroimagerie, CHUV, University of Lausanne, Switzerland, [4]Wellcome Trust Centre for Neuroimaging, University College London, United Kingdom, [5]Institut für Systemische Neurowissenschaften, Universitätsklinikum Hamburg-Eppendorf, Germany, [6]Weierstrass Institute for Applied Analysis and Stochastics, Berlin, Germany.

HIGHLIGHTS

PURPOSE: **Quantitative magnetic resonance imaging (qMRI)** helps reveal the biophysical properties governing MRI contrast. By eliminating instrumental biases and other contrast mechanisms influencing the signal amplitude, quantitative parameter maps can be derived and ultimately serve as *in vivo* biomarkers[1]. **Biases in proton density (PD) map estimation** include radio-frequency transmit (B_1^+) and receive (B_1^-) fields and T_2* weighting[2-5]. We focus on the T_2* bias in multi-echo fast low angle shot (FLASH) protocols, where the T_2* signal dependence is often neglected[5,6]. Although often pointed out as a potential limitation especially in high iron content areas[5,7,8], the extent and severity of this bias and the evaluation of correction strategies have not yet been fully reported.

RESULTS: Simulated FLASH multiparameter mapping datasets with increasing noise levels were analysed with the hMRI toolbox and various processing strategies for PD estimation. Without T_2* bias correction and with calibration to PD=69% in the WM, PD values were overestimated in the cortex (since $T_2*_{GM} > T_2*_{WM}$) and strongly underestimated in high iron content areas (globus pallidus, red nuclei, substantia nigra).

CONCLUSIONS: **T_2* bias correction is necessary to increase the sensitivity and specificity of qMRI** in these areas. All methods taking T_2* weighting bias into account are effective. However, method (2) shows lower SNR (relies on a single echo), while methods (1) (with T_2* correction) and (3) perform similarly.

METHODS

SIMULATIONS: Multi-echo FLASH images (multiparameter mapping protocol[7]) with PD and T_1-weighting (8 TE values equally spaced between 2.34 and 18.72ms, TR=25ms, FA=6° and 21° respectively) were simulated using the Ernst equation (assuming perfect RF spoiling[9]), SoS combination of the individual receiver coil signals and Gaussian noise added to the individual coil images (spatially variable SNR). R_2*, R_1, PD and B_1^+ maps generated using the hMRI toolbox[10] (single subject dataset) were adaptively denoised[11,12] and masked to serve as noise-free inputs to the simulation and as references to evaluate deviations of the PD and R_2* map estimates. Synthetic coil sensitivities were generated using the Biot-Savart law[13,14] for 48 coil elements distributed on a 24cm-diameter sphere (excluding neck aperture in the head coil).

PROCESSING: **hMRI toolbox[10]** with ESTATICS model[15] to estimate R_2* maps and rational approximation of the Ernst equation[6] to estimate R_1 and A (biased PD) maps. A maps accounted for B_1^+ bias only (based on the B_1^+ map input to data simulation). T_2* correction factor[2] (optional), Unified Segmentation B_1^- bias correction[7,16] and calibration (PD_{WM} = 69%[17]) were then applied to generate quantitative PD maps.

The A maps were derived either from:

(1) the first 6 echoes of the PD-weighted images, averaged to increase SNR,

(2) the first PD-weighted echo only (to reduce T_2* bias),

(3) extrapolation (TE=0) of the signal decay in the PDw images .

An optional T_2* correction factor ($1/mean(exp(-TE_i \cdot R_2*))$) was applied voxel-wise to the A map before B_1^+ bias correction (ESTATICS-estimated R_2* and *mean* calculated across TE_{1-6} (1) or TE_1 alone (2). No additional correction factor was required for (3). All the above methods are implemented in the hMRI toolbox[10].

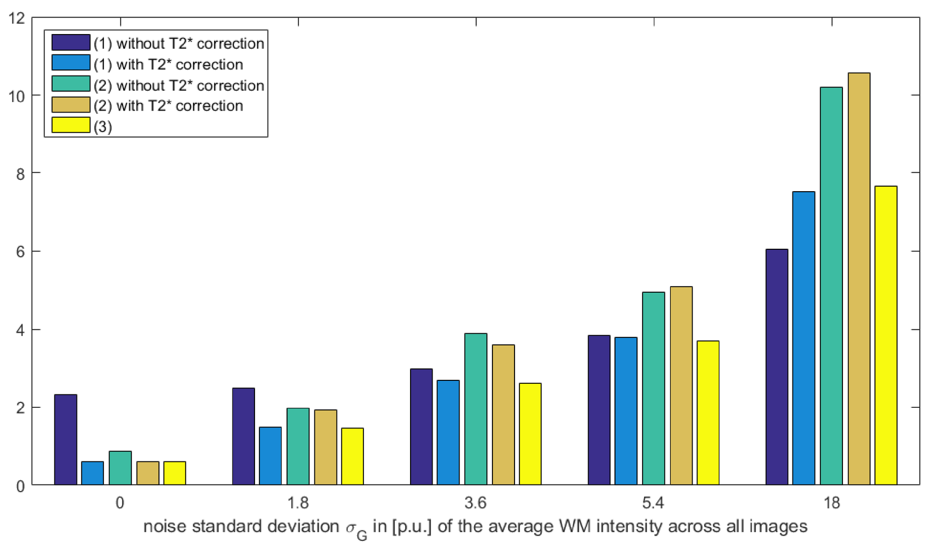

FIGURE 5 - Standard deviation of the PD error (200*(PD -PD)/(PD +PD) in p.u.) in the WM for each method and increasing noise levels. Due to the calibration procedure, the average error in the WM is 0. With T_2* correction, method (1) achieves better than method (2) due to the higher SNR of the input PD-weighted images (average over 6 echoes versus single echo). The T_2* correction reduces the error in the PD estimate as long as the noise added by the R_2* estimate is smaller than the variations due to T_2* bias. TE=0 extrapolation (method (3)) performs similarly to method (1) with T_2* correction.

REFERENCES

1. Weiskopf *et al.* Curr Opin Neurol. 2015;28(4):313-22. **2.** Neeb *et al.* Neuroimage. 2006;31(3):1156-68. **3.** Volz *et al.* MRM 2012;68(1):74-85. **4.** Abbas *et al.* MRM 2014;72(6):1735-45. **5.** Mezer *et al.* HBM 2016;37(10):3623-35. **6.** Helms *et al.* MRM 2008;59(3):667-72. **7.** Weiskopf *et al.* Front Neurosci. 2013;7:95. **8.** Callaghan *et al.* Neurobiol Aging. 2014;35(8):1862-72. **9.** Preibisch & Deichmann MRM 2009;61(1):125-35. **10.** hMRI-Toolbox: http://www.hmri.info & Poster #2095. **11.** Mohammadi *et al.* Preprint no. 2432, WIAS, Berlin, 2017, DOI 10.20347/WIAS.PREPRINT.2432 **12.** Tabelow *et al.* OHBM 2016, Geneva. **13.** Guerquin-Kern *et al.* IEEE Trans Med Imaging. 2012;31(3), 626-636. **14.** Matlab Framework for MRI Simulation and Reconstruction: http://bigwww.epfl.ch/algorithms/mri-reconstruction/code_v1-0.zip **15.** Weiskopf *et al.* Front Neurosci. 2014;8:278. **16.** Weiskopf *et al.* Neuroimage. 2011;54(3):2116-24. **17.** Tofts PS, Quantitative MRI of the brain (chapter 4). John Wiley & Sons, Ltd, Chichester, UK. **18.** Ellerbrock & Mohammadi HBM 2017, doi: 10.1002/hbm.23858. **19.** Tabelow *et al.* ISMRM 2017, Honolulu.

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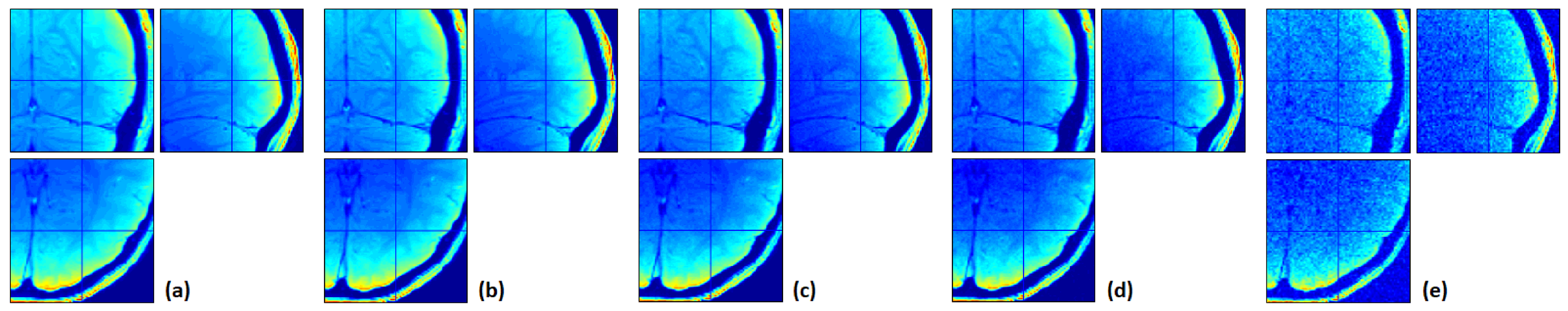

FIGURE 1 - **Simulated PD-weighted images** (TE=11.70ms) with increasing noise levels. (a) σ_G = 0%, (b) σ_G = 1.8%, (c) σ_G = 3.6%, (d) σ_G = 5.4%, (e) σ_G = 18%. The standard deviation of the added Gaussian noise σ_G is expressed in p.u. (%) of the average signal measured in the white matter across all (PD-weighted and T_1 -weighted) simulated echoes.

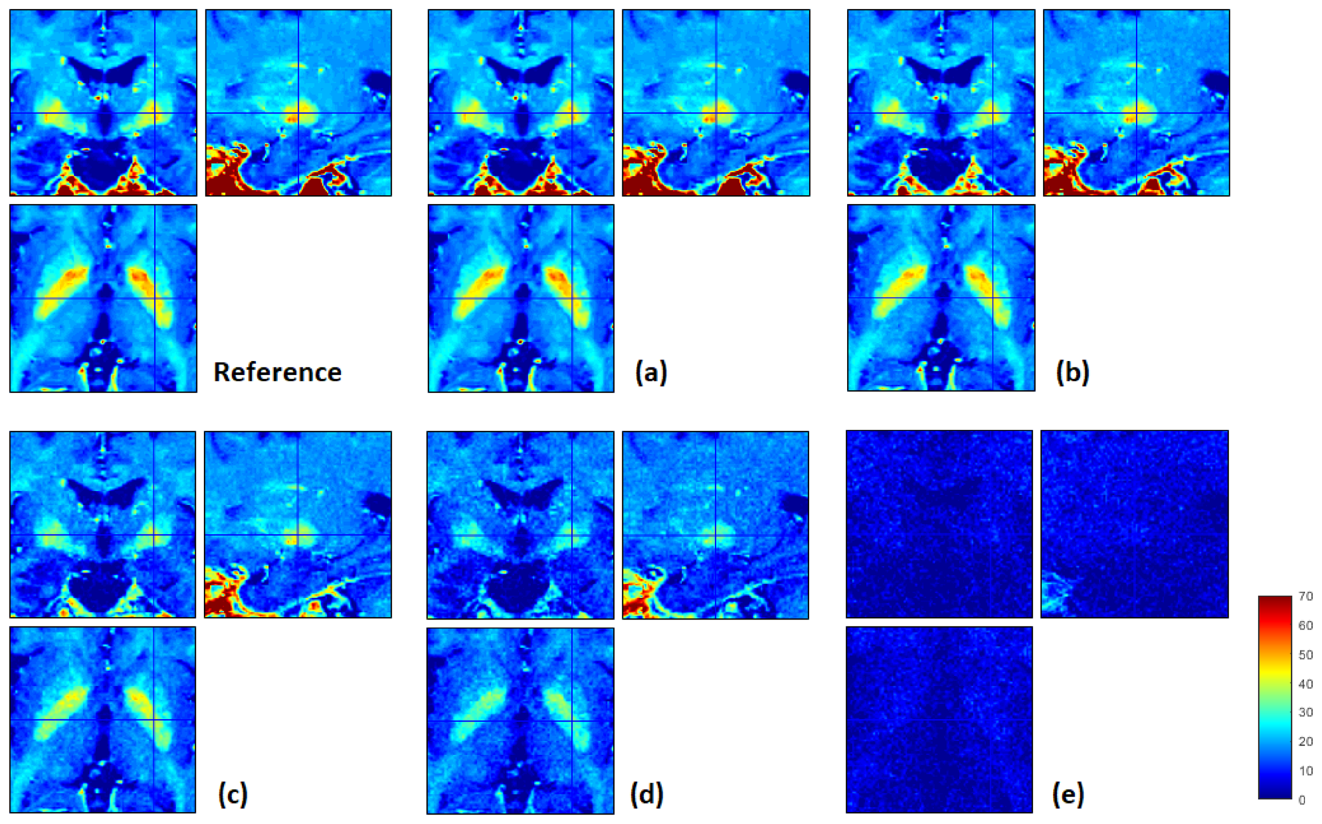

FIGURE 2 - **R_2* ESTATICS estimation.** R_2* reference image used for simulations and R_2* ESTATICS estimates derived from images with increasing noise levels: (a) σ_G = 0%, (b) σ_G = 1.8%, (c) σ_G = 3.6%, (d) σ_G = 5.4%, (e) σ_G = 18%. All maps are equally scaled between 0 and 70 s^{-1}. As expected, the increasing noise level leads to increasingly underestimated R_2* values (noise floor effect due to the central chi-distributed noise in the SoS combined images)[18].

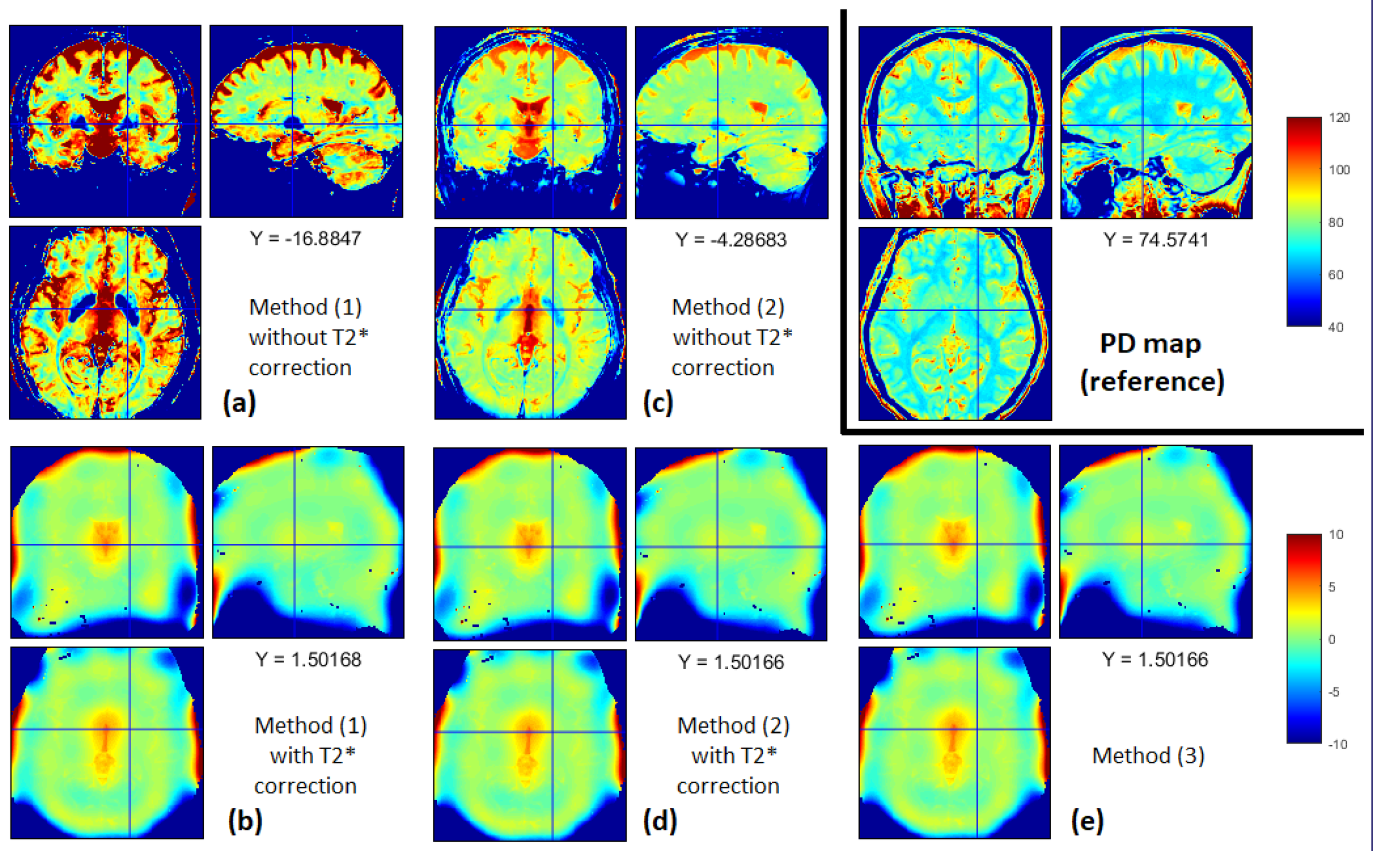

FIGURE 3 - **PD map estimation in the absence of noise.** PD reference image (% water content) used for simulations (top right) and PD estimation error ($200*(PD_{est} - PD_{ref})/(PD_{est} + PD_{ref})$ in p.u.) for each method (a-e). All methods taking the T_2* weighting bias into account (b,d,e) provide good and almost identical results. Residual error is mostly related to the B bias field imperfect correction (smooth variation across the volume). Errors outlined by anatomical details are likely related to the approximation of the Ernst equation used to estimate the quantitative maps[5]. Values (Y) within the globus pallidus (blue cross intersection) are reported under each sagittal view for comparison.

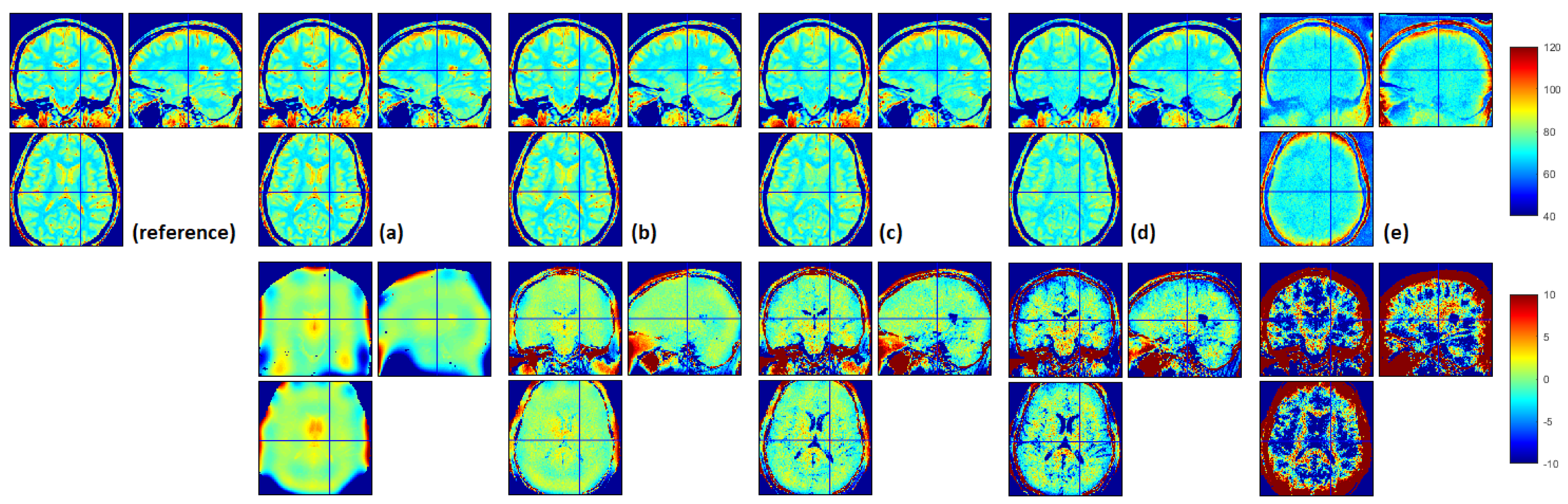

FIGURE 4 - **PD map estimation in the presence of increasing noise levels.** PD reference map, PD maps estimated with method (3) (top row) and corresponding PD error relative to the PD reference map (bottom row). Noise levels: (a) σ_G = 0%, (b) σ_G = 1.8%, (c) σ_G = 3.6%, (d) σ_G = 5.4%, (e) σ_G = 18%. The results for methods (1) & (2) with T_2* correction were very close to method (3) (data not shown), except for the lower SNR observed for method (2) (calculation relying on a single echo).

Cyclotron research centre

LIÈGE université GIGA institute

Contact : e.balteau@uliege.be | The hMRI toolbox : http://hmri.info