# *In vivo* Chloride Quantification with Partial Volume Corrected $^{35}$Cl-MRI

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**TARGET AUDIENCE** Scientists and physicians interested in the field of non-proton MRI

**PURPOSE** Chloride plays a key role in many physiological processes [1]. Thus, a non-invasive determination of the chloride concentration by $^{35}$Cl-MRI is desirable. However, the $^{35}$Cl-nucleus experiences extremely fast transverse relaxation [2] and an *in vivo* signal which is reduced by six orders of magnitude compared to protons ($^{1}$H). Nevertheless, the feasibility of *in vivo* $^{35}$Cl-MRI of human muscle and brain has recently been demonstrated [2]. For $^{35}$Cl-MRI pulse sequences that enable ultra-short echo-times and high SNR efficiency such as 3D density adapted radial or twisted projection imaging [3] are necessary. Still, only resolutions of (>6mm)$^3$ are achievable within acceptable acquisition times. Additionally, the applied acquisition schemes and fast $T_2$*-relaxation lead to large full widths at half maximums (FWHM) of the *point spread functions* (PSF). The large voxel dimensions and the additional broadening of the PSF result in partial volume (PV) effects that decrease the accuracy of quantitative concentration measurements. For sodium ($^{23}$Na) MRI a partial volume correction (PVC) algorithm, based on a method for positron emission tomography by Rousset et al. [4], was presented that enabled improved quantification [5]. This method was now applied to *in vivo* $^{35}$Cl-MRI.

**METHODS** A phantom was used to test the correction and quantification performance of the PVC. A silicone-caoutchouc cushion filled with 2% w/w agarose gel and different NaCl-concentrations (25-150 mmol/L) [6] was used for quantification of the signal (Fig 1.B). Imaging was conducted on a 7T MR system (Magnetom 7T, Siemens AG, Healthcare Sector, Erlangen, Germany), where image acquisition was performed with a density adapted projection pulse sequence (3D-DAPR [7]). For phantom imaging the following parameters were applied: TR/TE=150ms/0.5ms, 10000 projections, Θ=90°, nominal resolution: (6mm)$^3$; $T_{Acq}$=25min (Fig. 1.B). Additional data for a phase sensitive $B_1$-correction [8] and a separate $B_0$-correction were obtained.

*In vivo* quantification: PVC as described in the previous $^{23}$Na-MRI approach [5] with relaxation weighting of the PSF (brain matter (BM): $T_{2s}^*$=1.2 ms, $T_{2l}^*$=7 ms and $T_1$=9.2 ms [2]; CSF: $T_2^*$=$T_1$=35ms) was applied to $^{35}$Cl-data sets of three healthy volunteers with two experiments each. Data sets were acquired with a 3D-DAPR pulse sequence (TR/TE=125ms/0.4ms, 6000 projections, (6.5mm)$^3$, Θ=90°, $T_{Acq}$=12min 30s, Fig. 2.A) with additional correction of $B_1$- and $B_0$-inhomogeneity, as in the phantom study. The chloride tissue concentration (CTC) was calculated for two separate CSF compartments (lateral ventricles ($CSF_i$) and sulci ($CSF_o$), same expected CTC) and for BM. Signal of the reference cushion (Fig. 2.B) was also PV-corrected to prevent underestimation of the calibration. Structural information of the cushion was obtained with a proton 3D-GRE (TR/TE=8.1ms/4.88ms, Θ=10°, (1mm)$^3$) and segmented manually. Correction behavior of the two CSF compartments with the calculated difference $\Delta_{CSF}$ between $CSF_i$ and $CSF_o$ was used as an intrinsic correction control.

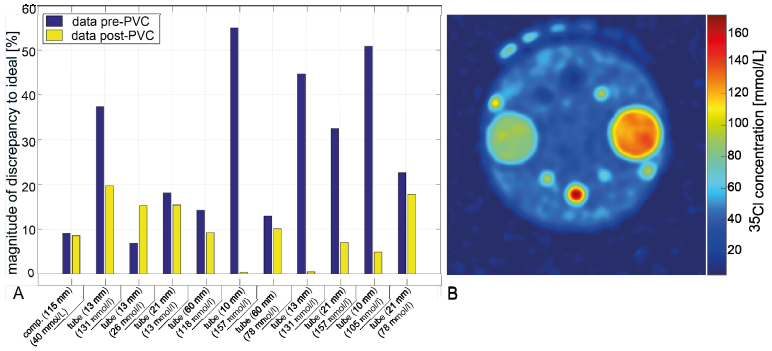


***Fig.1**:(**A**) Plotted magnitude of discrepancy for phantom data before (blue) and after correction (yellow), an improvement in quantification accuracy is seen for post-correction data. (**B**) Used $^{35}$Cl-data ((6mm)$^3$, TR=150ms, TE=0.5ms) for quantification.*

**RESULTS** Performance of phantom PVC and calibration was directly verified with known $^{35}$Cl-concentrations of eleven reference tubes (Fig.1.B). The magnitude of discrepancy of obtained to expected concentration values before and after correction was calculated and plotted (Fig. 1.A). A mean reduction of discrepancy of 16% is seen after correction. *In vivo* data showed a cutback of mean $\Delta_{CSF}$ from 35.8% to 5.4% and an upward correction for both CSF values (Tab.1). Brain matter CTC was shifted downward from 32 mmol/L to 27 mmol/L (-15.6%).

***Tab. 1:** Mean values ± std. of CTC for in vivo experiment*

| | $CSF_o$ [mmol/L] | $CSF_i$ [mmol/L] | mean diff. $\Delta_{CSF}$ [%] | BM [mmol/L] |
|---|---|---|---|---|
| **Pre-PVC [mmol/L]** | 35 ± 2 | 54 ± 4 | 35.8 ± 2.7 | 32 ± 3 |
| **Post-PVC [mmol/L]** | 98 ± 7 | 100 ± 4 | 5.4 ± 3.1 | 27 ± 3 |

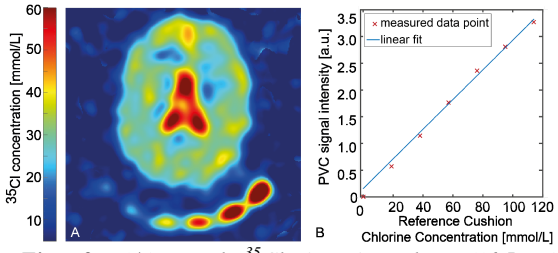


***Fig. 2:** (**A**) Used $^{35}$Cl in vivo data ((6.5mm)$^3$, TR/TE=125ms/0.4m) with signal of reference cushion (zoomed FOV 228x228x228 mm).(**B**) result of fit (blue) with PV-corrected data of calibration cushion (red).*

**DISCUSSION** The PV effects were reduced by a PVC algorithm that allowed a strongly improved quantification for $^{35}$Cl-MRI. For phantom measurements, heavy PV influence was seen (mean discrepancy 27%). True values were recovered, quantified and verified with known concentration values. Results of the phantom study showed correction capability of the algorithm and quantification capacity of the reference cushion. For *in vivo* measurements the intrinsic correction control indicates good correction behavior: CSF CTC values were shifted closer together and the theoretical $^{35}$Cl-concentration for both CSF compartments was met (99-110 mmol/L). BM CTC was corrected downward as expected and was lower than previously reported values [2], where PV effects were not considered. However, the calculated CTC might be underestimated due to the fast transverse relaxation of $^{35}$Cl in tissue.

**CONCLUSION** Correction capability of a previously introduced PVC algorithm for $^{23}$Na-MRI [5] was demonstrated for $^{35}$Cl-MRI where much stronger PV influence due to larger voxel sizes is expected. The correction and quantification approach allowed absolute $^{35}$Cl-quantification in the human brain, where PV-bias was strongly reduced.

**REFERENCES**

**[1]** Jentsch et al., *Physiol Rev 2002 (2): 503-68* **[2]** Nagel et al., *Radiology 2014 (2): 585-95* **[3]** Konstandin S, Nagel AM., *MAGMA 2014 (27):5-19,* **[4]** Rousset et al., *J Nucl Med 1998(5):904-911, 1998,* **[5]** Niesporek et al., *Proc. Intl. Soc. Mag. Reson. Med. 22 (2014), p. 1523* **[6]** Mirkes et al., Magn *Reson Med 2014; 10.1002/mrm.25096* **[7]** Nagel et al., *Magn Reson Med 2009 (62):1565-73* **[8]** Morell, *Magn Reson Med 2008 (60):889-94*