INTRODUCTION: Due to the relatively low spatial resolution, arterial spin labeling (ASL) images are strongly affected by partial volume effects (PVE). This can make the qualitative analysis of ASL images difficult and it also significantly decreases the accuracy of cerebral blood flow (CBF) quantification. The CBF can be corrected for by using gray matter (GM) and white matter (WM) tissue segmentation of high-resolution $T_1$-weighted images as proposed by Aslani et al. The main drawback of this method is the need for precise knowledge of the partial volume ratios. However, the segmentation of $T_1$-weighted images is very difficult at the border of GM and WM. Moreover, ASL images contain susceptibility induced deformations typical for EPI images and thus a correct registration with $T_1$-weighted images is not always possible. Hence, the PVE correction using segmented $T_1$-weighted images can introduce artifacts. In this study, we analyze an alternative method to obtain the partial volume ratios through the longitudinal magnetization relaxation times obtained from a Look-Locker sampling acquired in a multiple inversion time (TI) ASL sequence.

METHODS: Data acquisition: Images of two healthy volunteers were obtained with a clinical 3T Philips Achieva MR scanner (part of the Philips Ingenity PET/MR system) using a standard head-coil. The acquisition protocol consisted of three EPISTAR PASL sequences and a 3D TFE $T_1$-weighted sequence. The common parameters of the ASL sequences were TR/TE = 4000/25 ms, label thickness/gap = 150/20 mm, FOV = 192x192 mm$^2$, matrix = 64x64, 4 slices (6 mm/2 mm gap) and 30 averages. Two multi-TI Look-Locker sequences with $T_1$/ATI/TI = 50/300/3650 ms and flip angles $\alpha = 30^\circ$, respectively $10^\circ$, were acquired followed by a single-TI ASL with $\alpha = 90^\circ$ and TI = 1700 ms. A 3D $T_1$-weighted sequence with the following parameters was acquired: TR/TE = 8.2/3.7 ms, FOV = 256x256 mm$^2$, 150 slices, voxel size = 1x1x1 mm$^3$, $\alpha = 8^\circ$. Image processing: The $T_1$-weighted image was aligned to the single-TI ASL sequence using a 3D rigid registration and it was segmented to GM/WM/CSF with the SPM toolbox. The ratios $P_{GM}$, $P_{WM}$ and $P_{CSF}$ describing the tissue partial volume in ASL pixels were calculated (this method was denoted PV-SEG). Partial volume estimation: The effective $T_1$-relaxation times $T_{1,\alpha}$ and $T_{1,90}$ were estimated for each voxel from the control images of the Look-Locker sequence. Because of the acquisition at multi-TI, the effective relaxation time $T_{1,\alpha}$ depends on the flip angle $\alpha$: $1/T_{1,\alpha} = 1/T_{1,-\ln cos(\alpha)}/ATI$ [1]. Due to $B_0$ field inhomogeneities, the real flip angle is not equal to the expected value. However, it can be estimated from $T_{1,\alpha}$ and $T_{1,90}$ using Eq. [1] which yields also a corrected estimate of tissue $T_1$-relaxation time in every voxel. The distribution of relaxation times in all measured voxels was analyzed in order to obtain relaxation times of GM and WM. This was done using the EM algorithm by fitting a mixture of 4 Gaussians to the data [2]. An estimation of CSF relaxation time is difficult due to low number of CSF voxels and thus a literature value of 4300 ms was used [3]. The following model is valid for the control images $M=M_0\sum P_i d_i (1-exp(-T/T_i))$ [2], where $M_0$ is the equilibrium magnetization, $P_i$ the tissue specific partial volume ratios and $d_i$ the water density (0.73, 0.89 and 1.0 for WM, GM and CSF, respectively) and $T_i$ the inversion times. With the knowledge of tissue relaxation times $T_{1,\alpha}$, the partial volume ratios $P_i$ can be estimated by solving Eq. [2] in the least-squares sense (this method was denoted PV-REL) [2]; see Fig. 1. Partial volume correction: We assume smoothness of the GM and WM perfusion. For every pixel $x$, the control/label difference $\Delta M$ is then equal to: $\Delta M(x) = M_{GM}(x)P_{GM}(y) + M_{WM}(x)P_{WM}(y) + M_{CSF}(x)P_{CSF}(y)$, where $y$ is in a 3x3 square neighborhood of $x$. This system of equations can be solved [4] giving the PVE corrected values of $M_{GM}$ and $M_{WM}$. The PVE correction was performed for the single-TI ASL and multi-TI (for TI = 1550 ms only) data. In both cases, the partial volume ratios PV-SEG and PV-REL were used. Validation: The mean fitting error $|\Delta M(x) - M_{GM}(x)P_{GM}(y) - M_{WM}(x)P_{WM}(y) - M_{CSF}(x)P_{CSF}(y)|$, was calculated to quantify the discrepancies between the estimated values and the ASL images. The corrected perfusion maps $M_{GM}$ are supposed to be smooth with lowvariation between different brain regions. The mean total variation on the $M_{GM}$ and $M_{WM}$ was thus computed to verify this assumption for both methods (PV-SEG and PV-REL). Finally, the CBF was quantified on the measured images and on $M_{GM}$ of both methods. The mean CBF was computed in regions with over 20% and 90% of GM partial volume.

RESULTS: The root mean square fitting error for the two subjects was 24.4%/20.2% (single-TI/multi-TI) lower for PV-REL compared to PV-SEG. The total variation was 24.7%/18.6% (single-TI/multi-TI) smaller on $M_{GM}$ and 9.8%/19.2% smaller on $M_{WM}$ for PV-REL than for PV-SEG. The mean CBF in the region with GM partial volume over 20% on the uncorrected images was 42.8/37 ml/100 g/min (single-TI/multi-TI); 52.1/45.8 ml/100g/min on $M_{GM}$ for PV-SEG and 59.1/53.3 ml/100g/min on $M_{GM}$ for PV-REL. The CBF values in the region with GM > 90% was 56.2/52 ml/100g/min for the uncorrected images; 53.5/49.9 ml/100g/min for $M_{GM}$ for PV-SEG and 59.1/56.3 ml/100g/min for $M_{GM}$ for PV-REL.

DISCUSSION: The PV-REL has significantly lower fitting error on both single-TI and multi-TI images, see Fig 2. In addition, there is higher variation of the corrected GM and WM perfusion maps on both types of images in the PV-SEG results, see Fig 3. The CBF measurements at GM fraction over 20% clearly indicate that the real GM CBF is, as expected, higher than the uncorrected value. For regions with GM over 90% the uncorrected and GM corrected value by PV-REL are getting closer as a result of correct PV compensation. However, the corrected values for PV-SEG are lower than expected as a result of incorrect estimation of PV ratios. In conclusion, the partial volume ratios obtained using the Look-Locker sequence (PV-REL) provides better estimation of the position of GM and WM structures. The effect on absolute CBF quantification looks promising as well. However, this needs to be analyzed more thoroughly in further studies.