Introduction: The ASL (Arterial Spin Labeling) signal decays with T1, resulting in low signal intensities at long TIs (inflow times). An inflow curve with long BAT (bolus arrival time) therefore has lower maximum signal intensity compared to one with short BAT, even though the represented perfusion value is the same (cf. fig. 1). Usually the inflow curve is sampled with an equal number of averages at every TI. Meaning that longer TI suffer from lower SNR due to labeling decay. Simulations of the general kinetic model [1] show, that this reduction in signal intensity increases the relative error of the fitted perfusion value with increasing BAT [2]. Recently, we have shown that by redistributing the number of acquisitions per TI, SNR can be increased for longer TIs [2,3] (keeping the overall scan time constant). Such a correction is of high clinical relevance in cerebrovascular diseases: here, patients with high graded stenosis of the extra- or intracranial cerebral vessels will show prolonged BAT with or without corresponding hypoperfusion according to the degree of collateral flow. In those patients a correction for prolonged BAT will identify high signal intensity and thus avoid false positive results. In this paper, we present various redistribution schemes where the number of averages is reduced at short TIs and increased at long ones. The impact of the redistribution on perfusion estimation in cases of long BAT is studied and compared to the standard acquisition method.

Methods: Five healthy volunteers (4 M, 1 F, age: 27-39 y) as well as two patients participated in the study (#1: F, 74 y, no pathological findings; #2: M, 57 y, occlusion of the left internal carotid artery and a left middle cerebral artery stroke 6 months prior to imaging). 3T whole body scanners were used with a 20 channel head coil (Siemens Magnetom Verio) and in the case of the patient with ICA-occlusion with a 12 channel head coil (Siemens Magnetom Trio). An optimized FAIR PASL pulse scheme (post labeling saturation, background suppression, Q2TIPS) was used in combination with a 3D-GRASE readout [4]. Voxel wise spatial resolution of 3.5 mm. Eight partitions were obtained, orientated around the corpus callosum. Partial Fourier of 6/8, EPI factor of 64 and a turbo factor of 6 were used. TE was 42.14ms and TR 2800ms. The maximal bolus length was set to 1400ms, being truncated earlier by the Q2TIPS for TIs < 1400ms. A time series of 10 TIs starting at 250ms to 2500ms with 250ms spacing was acquired seven times. Three types of distribution modes (details found in [2,3]) were applied to the data, keeping the total number of acquisitions the same (equal mode (3,3,3,3,3,3,3,3,3,3), linear mode (1,2,2,2,3,3,4,4,4,5) and quadratic mode (1,1,1,2,2,3,4,4,5,7)). This way the three averaging modes were applied to the same data set and could be reliably compared. No registration of the single measurements was necessary. TI weighted images were obtained to generate masks for gray and white matter segmentation. Voxel wise fitting of perfusion and BAT was done according to the Buxton model [1] with the fitting routines of MPFIT [5]. The initial error on every TI after adaptive averaging was calculated via the background noise and is regarded in the fit. A signal threshold of 10 was used for fitting. The results were analyzed by comparing the relative error of the perfusion values for different BATs. The allowed range for the BAT fit was 1 to 1500ms. The perfusion values and their errors (from 20 to 160 ml/100g/min in steps of 10 ml/100g/min for BAT values from 1 to 1500ms in 100ms distribution modes). Additionally the number of voxels within different BAT ranges were counted and compared among volunteers and patients.

Results: The relative error of the perfusion increases with increasing BAT (fig. 2) and decreases with increasing perfusion values. When quadratic averaging is used, this error can be significantly reduced – especially at long BATs. In grey matter for BATs below 300ms, equal averaging has the lowest relative error. For BATs of 300 to 500ms, the relative error does not differ much between the averaging modes. For BATs longer than 500ms, the relative error first for linear and then for quadratic averaging becomes higher than for equal averaging. For BATs below 1000ms the relative error of perfusion values is below 20% in areas with perfusion values from 30 to 60 ml/100g/min and below 10% in areas of perfusion values >60 ml/100g/min with quadratic averaging. The difference of the relative error between equal and quadratic mode amounts to 10%. For white matter, similar results were found. Comparing patients and volunteers we found comparable results for the relative perfusion error. However, the number of voxels with an increased BAT found in the images of the patients was much higher than in volunteers. Figure 3 shows the percentile grey matter voxel distribution at the different BATs for the five volunteers and the two patients. The number of voxels with long BATs is higher for the patient with steno-occlusive disease and even further increased for the elderly patient.

Discussion and Conclusion: The results show that with the quadratic mode the SNR loss due to T1 decay at long TIs can be partly compensated, resulting in a reduced perfusion error. This is of great importance when multi TI experiments are extended to TIs above 3000ms or, as shown here, in patients with prolonged BATs. In these patients, standard perfusion imaging (i.e. equal averaging) can result in hypointense areas and hypoperfusion could be reasoned. In recent studies, imaging at inflow times above 3000ms showed that the perfusion values are in fact normal in these areas and only the BATs are prolonged. Thus, imaging at these long TIs might be necessary to avoid erroneous conclusions. The quadratic average distribution ensures sufficient SNR when imaging at these long BATs and does thereby not increase scan time compared to standard equal averaging. For a sequence comparable to the volunteer study, which directly uses quadratic averaging the scan time is under 3 min when obtaining 8 partitions and under 6 min when obtaining 24 partitions.

In summary, a quadratic acquisition distribution holds the potential to speed up and improve quantification of perfusion measurements and diagnosis, especially for patients with prolonged BATs. The method is straightforward to implement. Thus, it can easily be applied in every day routine of multi TI ASL measurements and should be part of the clinical protocol.

References: