On the Feasibility of White Matter Arterial Spin Labeling Measurements

P. van Gelderen, J. A. de Zwart, J. H. Duyn

Advanced MRI section, LFMI, NINDS, National Institutes of Health, Bethesda, Maryland, United States

Introduction

Cerebral perfusion can be used to distinguish between normal and compromised brain function, and its measurement has many important applications in the study of brain function and pathology. MRI-based arterial spin labeling (ASL) techniques have been used (1-3) to measure perfusion successfully in various applications (e.g. (4-7)). Despite their substantial clinical value ASL techniques have a number of drawbacks, such as limited coverage, low SNR and sensitivity to the transit time. An additional complication is the inherently high contrast between gray matter (GM) and white matter (WM), as WM has an approximately five fold lower perfusion. This makes the typically low resolution perfusion measurements sensitive to partial volume and blurring effects. As a result GM signal is mixed into the WM, artificially increasing the measured WM perfusion. On the other hand the longer transit times in WM tend to decrease the WM signal. Both effects complicate the measurement of WM perfusion, which may explain why there is little consistency in the reported MR literature values (8) or with the assumed gold standard of autoradiography (9). Here we discuss the SNR, image resolution and transit time issues in order to estimate WM perfusion reliability. Supporting 3T data is shown as well.

Image Resolution

The limited image resolution results in mixing of the much stronger GM signal into the WM. This can be a result of both partial volume effects, since a voxel may contain a mix of tissues, and of blurring, where signals originating in one voxel are mixed into their neighboring (or farther) voxels by the imaging process. A simulation of these effects is shown in Table 1 and Fig. 1, demonstrating the contamination of WM signal by the neighboring GM. To limit this effect to less than 50% of the WM signal, which is about 0.2 times the GM signal, a resolution on the order of 1.9mm is necessary.

The simulation was based on a 1.1mm resolution 3D TSI (10) scan resulting in a GM and WM map. The GM was set to one, the WM to zero and then this image was blurred to various resolutions and the signal amplitudes in the GM and WM voxels were averaged.

Transit time

To estimate the WM transit times, bolus tracking experiments were performed on six volunteers in a 3T GE scanner with a 16-channel receive coil and a receiver system built in-house. A twelve-slice EPI series was acquired at 1.5mm resolution, with SENSE rate 2, 1s TR, 40ms TE, 180 repetitions. The fitting of gamma-variate curves resulted in a voxel-by-voxel estimate of the arrival time of the bolus. See Fig. 2 for an example bolus amplitude and arrival time maps.

Although this timing information does not result in absolute ASL transit times, it does indicate the relative voxel to voxel differences. The spread in bolus arrival was several seconds, with WM mostly showing a later arrival, see Fig. 3. This shows that the transit time, in at least part of the WM, is often several seconds longer than the average GM transit time.

ASL SNR estimation

The labeled spins decay during the transit time from the labeling site to the exchange (and image) site, while the exchange results in an increase in accumulated label over time. This can be modeled as:

$$L(t)=(t-t_t)\cdot e^{-t/T_1};\ t>t_t$$

which is illustrated in Fig. 3, showing the loss of label with longer transit times.

Assuming a 100% labeling efficiency and complete suppression of the blood signal, the maximum (ie. at optimal labeling time) perfusion SNR in a pulsed ASL experiment can be expressed as:

$$SNR_{p,max}=T_1\cdot f/\lambda\, e^{-1}\, e^{-t_t/T_1}\cdot SNR_{base}\cdot\sqrt{N}\cdot 2\cdot\sqrt{0.5}$$

The following parameters were used: T_1= 1500ms, f_{WM} (perfusion fraction)= 0.003ml/g/s (= 0.18ml/g/min), f_{GM}= 0.013ml/g/s (= 0.8ml/g/min) (11, 12), λ_{WM} (partition coefficient)= 0.82ml/g, λ_{GM}= 0.98ml/g (13), N (averages)= 92 (i.e. a 10min scan time), $SNR_{base,WM}$= 13, $SNR_{base,WM}$= 22 per unit volume (values measured with a 16 channel array coil at 3T).

Fig. 4 shows the SNR as function of resolution at a number of transit times. The resulting $SNR_{p,MAX}$ for the desired 1.9mm resolution as function of transit time t_t, is printed in Table 2. While the perfusion signal in GM at a 0.9% relative amplitude is easily detectable, the WM amplitude is much lower, even for a short transit time of 1s. Longer transit times result in more label decay, diminishing the relative amplitude to below 0.1%, which is approximately the noise level for this type of experiment, even with the use of a sensitive 16-channel receive array.

ASL experiments

FAIR (3) ASL measurements were performed on 7 volunteers on the same 3T scanner (see above). A 1.9mm resolution EPI was chosen with a TE of 27ms, TR of 3.2s, 10min. scan time. Three scans were taken with labeling delays of 1.5, 2 and 3s. The average perfusion signal in GM and deep WM was calculated using anatomically defined masks. Table 3 reports the resulting SNR and relative amplitudes, showing good correspondence with the theory. The WM perfusion SNR is less than one for all labeling times. Fig. 6 shows an example for one volunteer at the three labeling times, scaled to obtain approximately the same image intensity in GM for all three.

Discussion

FAIR ASL SNR in WM is insufficient for a reliable and practical WM perfusion measurement with the current state of the technology. The WM perfusion fraction is low compared to GM and the transit times are long, probably up to several seconds longer than GM, resulting in a very low perfusion signal in at least part of the WM. Increasing the SNR by increasing the voxel size is not a viable option because it results in excessive contamination from the much stronger GM signals. A further complication is that the transit times appear quite heterogeneous, so that a correction would require a reliable transit time measurement at a similarly high resolution, running into the same SNR limitations. Some improvement may be possible using different labeling strategies and are field strength.

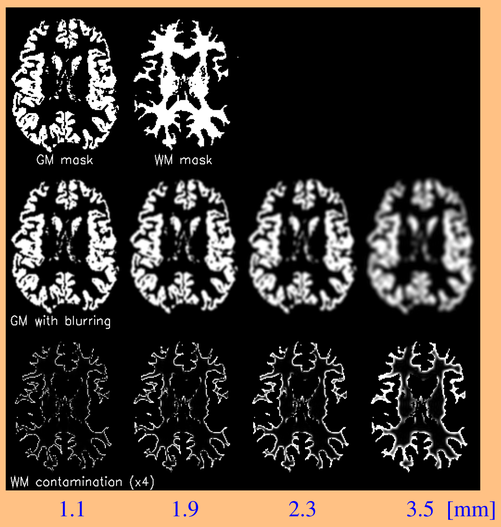

Figure 1. Simulation of the contamination of WM by the GM signals blurring into WM due to the limited image resolution. From top to bottom are shown: high resolution anatomical masks, the blurred GM and the resulting contamination to the WM at four image resolutions.

Table 1. Average GM and WM signals after blurring a simulated 1mm resolution perfusion map (based on a 3D anatomical scan) with the GM signal set to one and WM to zero.

Res [mm]	*1.1*	*1.9*	*2.3*	*3.5*
GM	0.86	0.78	0.72	0.63
WM	0.05	0.08	0.11	0.17

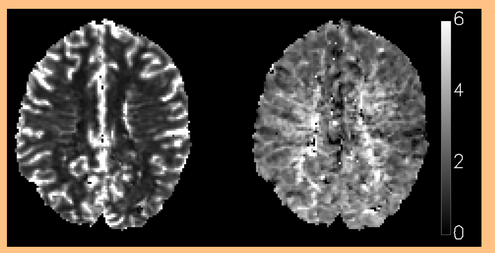

Figure 2. Example of a bolus tracking experiments, showing the fitted amplitude on the left and the arrival time of the bolus on the right (in seconds). A delay of several seconds is visible in parts of the WM.

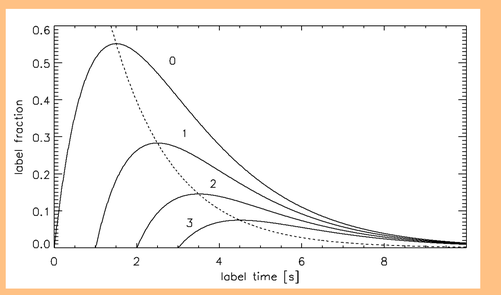

Figure 4. The labeled fraction as function of label time for transit times (t_t) of zero to three seconds, showing the decay of the label in the long transit time to WM.

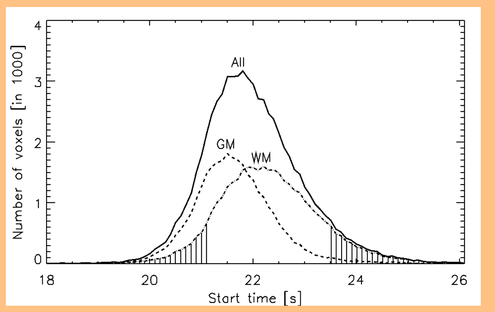

Figure 3. Distribution of arrival times in a bolus tracking scan, reflecting the start of the signal decrease. The shading indicates the fastest and slowest 10% of the WM.

Table 2. Theoretical relative perfusion amplitude and SNR in GM and WM for a 10min. 1.9mm resolution FAIR ASL scan.

Tissue	*GM*	*WM*	*WM*	*WM*
t_t[s]	0.75	1.0	2.0	3.0
SNR	10.1	1.3	0.7	0.3
amp [%]	0.91	0.21	0.11	0.05

Table 3. Average relative perfusion amplitude and SNR in GM and WM for a 10min 1.9mm resolution FAIR scan.

	amplitude [%]			*perfusion SNR*		
T_{label}	1.5	2.0	3.0	1.5	2.0	3.0
GM	0.87	0.86	0.53	9.37	9.37	5.74
WM	0.1	0.14	0.11	0.64	0.88	0.72

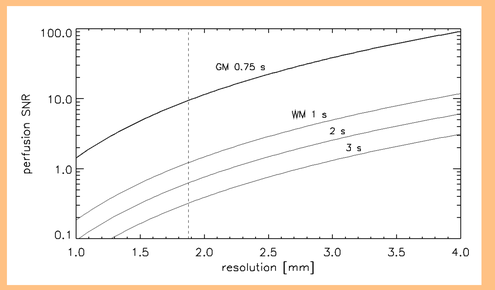

Figure 5. Estimated perfusion SNR as function of resolution for GM and WM, with the transit time indicated at the curves (see text for details).

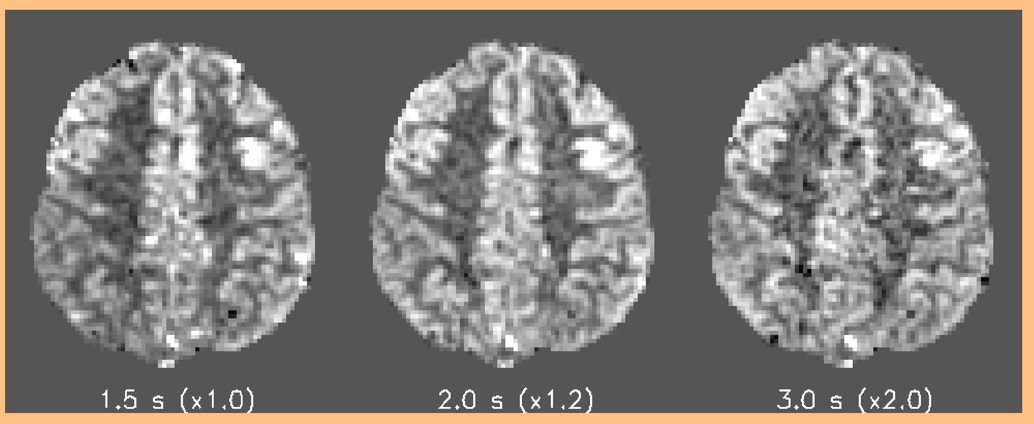

Figure 6. FAIR perfusion images at three label times, scaled with indicated factor. The WM signal is close to the noise in all three conditions for a ten minute scan. See text for experimental details .

References

1. J. A. Detre, J.S. Leigh, D.S. Williams, A.P. Koretsky. Magn Reson Med 1992 **23**, 37.
2. K. K. Kwong et al., Proc Natl Acad Sci U S A 1992 **89**, 5675.
3. S. G. Kim, Magn Reson Med 1995 **34**, 293.
4. X. Golay, J. Hendrikse, J. Van Der Grond, J Neuroradiol 2005 **32**, 321.
5. J. Kim, J. Whyte, J. Wang, H. Rao, K.Z. Tang, J.A. Detre. Neuroimage 2006 **31**, 376.
6. J. Wang et.al. Proc Natl Acad Sci U S A 2005 **102**, 17804.
7. J.A. Chalela , D.C. Alsop, J.B. Gonzalez-Atavales, J.A. Maldjian,S.E. Kasner, J.A. Detre. Stroke 2000 **31**, 680.
8. T. R. Steger, R. A. White, E. F. Jackson, Magn Reson Med 2005 **53**, 895.
9. M. Reivich, J. Jehle, L. Sokoloff, S. S. Kety, J Appl Physiol 1969 **27**,296.
10. V.N. Ikonomidou, P. van Gelderen, J.A. de Zwart , M. Fukunaga, J.H. Duyn. Magn Reson Med 2005 **54**, 373.
11. I. Law, H. Iida, S. Holm, S. Nour, E. Rostrup, C. Svarer, O.B. Paulson. J Cereb Blood Flow Metab 2000 **20**, 1252.
12. B. K. Owler et al., J Cereb Blood Flow Metab 2004 **24**, 17.
13. P. Herscovitch, M. E. Raichle, J Cereb Blood Flow Metab 1985 **5**, 65.