Effects of blood ΔR2* non-linearity on absolute perfusion quantification using DSC-MRI: Comparison with Xe-133 SPECT

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Introduction
Reproducible absolute quantification of cerebral blood flow (CBF) using dynamic susceptibility contrast MRI (DSC-MRI), is difficult, for example, due to partial volume effects (PVEs). In a previous DSC-MRI study, rescaling of the arterial input function (AIF) using a corrected venous output function (VOF) was shown to improve the correlation between CBF estimates obtained by DSC-MRI and Xe-133 SPECT [1]. However, in that evaluation a linear relationship between the ΔR_2* and contrast agent concentration in blood was assumed, while calibration measurements in whole blood have shown that a non-linear relation between ΔR_2*and contrast agent concentration exists [2]. In this re-evaluation of CBF data, we compared absolute CBF obtained using DSC-MRI and Xe-133 SPECT [1], using both a linear relationship and a non-linear relationship when applying the venous output function correction scheme to DSC-MRI data from healthy subjects.

Methods
Absolute CBF was measured in 20 healthy volunteers (45-80 years old) using DSC-MRI and Xe-133-SPECT on different occasions. In the Xe-133-SPECT experiment, xenon gas (500 MBq/l in air) was inhaled during 8 minutes and CBF was calculated using a bi-exponential analysis. In DSC-MRI, the first passage of the contrast-agent bolus was monitored using gradient-echo EPI (GRE-EPI), and CBF was calculated using Zierler's area-to-height relationship and the central volume principle. Deconvolution was performed using a block-circulant singular value decomposition algorithm [3], and a global arterial input function was obtained from middle cerebral artery branches in the Sylvian fissure region. The arterial and venous concentration time curves were calculated using a linear relationship (Eq. 1) as well as a non-linear relationship (Eq. 2) [4]:

$$\Delta R_2^*(t) = r_{2GdDTPA} AIF(t) \qquad [1]$$

where $r_{2GdDTPA}$ is the transverse relaxivity, assumed to be 5.9 $mM^{-1}s^{-1}$

$$\Delta R_2^*(t) = a_1 AIF(t) + a_2 AIF(t)^2 \qquad [2]$$

where a_1 was set to 7.62 $mM^{-1}s^{-1}$and a_2 to 0.57 $mM^{-2}s^{-1}$

For improved absolute quantification of the DSC-MRI-based CBF estimates, a rescaling of the arterial concentration time integral was introduced (based on the assumption that arterial and venous time integrals are identical) using an approximate VOF [1]. This rescaling was done on blood concentration time curves calculated using the linear relationship as well as the non-linear relationship. The tissue curves C(t) were in both cases calculated according to Eq. 1.

Results
DSC-MRI showed an average whole-brain CBF of 93 ± 30 ml/(min 100 g) using the linear relationship and 166 ± 40 ml/(min 100 g) using the non-linear relationship. The Xe-133-SPECT measurements resulted in a corresponding average whole-brain CBF of 40 ± 8 ml/(min 100 g). Figure 1 shows the individual data points, displayed as CBF(MRI) versus CBF(SPECT) using the two models. Under the assumption of proportionality between the two modalities, the relationship CBF(MRI)=2.4CBF(SPECT) (r=0.68) was observed using the linear relationship and CBF(MRI)=4.2CBF(SPECT) (r=0.62) using the non-linear relationship.

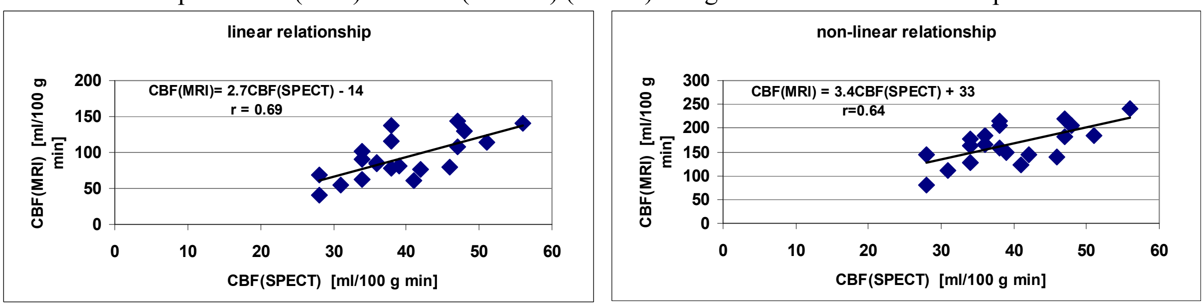

*Figure 1. Whole-brain cerebral blood flow estimates in ml/(min 100 g) obtained using Xe-133 SPECT and DSC-MRI in 20 healthy volunteers using the linear relationship (left) and the non linear relationship (right) between ΔR_2*and contrast agent concentration.*

Discussion
The observed degrees of correlation were similar when the linear and non-linear relationships were applied to the AIF and VOF from DSC-MRI. The quadratic relationship does not significantly influence the degree of correlation when proportionality was assumed. The small differences between the two models is probably due to PVEs present in both the VOF and the AIF, leading to reduced concentration of contrast agent and a smaller quadratic effect on ΔR_2*(t).

References: [1] Knutsson L et al. JMRI 2007;26:913-920 [2] van Osch MJ et al. MRM 2003;49:1067–1076 [3] Wu et al. MRM 2003;50:164-174 [4] Calamante F et al. MRM 2009;61:486-492