To what extent is dynamic susceptibility contrast MRI able to detect subtle blood-brain barrier leakage in cerebral small vessel disease?

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Abstract

Cerebral small vessel disease (cSVD) involves several pathologies affecting the small vessels, including blood-brain barrier (BBB) impairment[1]. Perfusion measures derived from dynamic susceptibility contrast (DSC) MRI have been shown to be sensitive to contrast extravasation over the BBB[2,3], and correcting for any leakage effects may be crucial to obtain reliable measures[4,5]. These correction methods might also be applicable to detect BBB leakage itself. This would be a time-efficient alternative to the lengthy dynamic contrast enhanced (DCE) MRI, which is currently most often used for the detection of BBB leakage. This study investigated to what extent DSC-MRI can measure subtle BBB leakage and whether contrast leakage effects are influenced by perfusion.

In vivo DSC and DCE data were collected from 27 subjects with a range in cSVD pathology severity and computer simulations of signal curves were performed to calculate to what limit BBB leakage can be quantified using DSC-MRI. DSC-derived leakage fractions were obtained using the Boxerman-Schmainda-Weisskoff method[4], both with and without arrival time correction[5] ($K2_{ATC}$ and $K2_{BSW}$, respectively). Additionally, we calculated three DSC-derived perfusion

measures: the cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT)[6,7]. The DSC-derived leakage factors $K2_{ATC}$ and $K2_{BSW}$ were compared with the DCE-derived leakage rate K_i, obtained from Patlak analysis[8]. Subsequently, differences in the outcome measures were assessed between white matter hyperintensities (WMH), gray matter (GM), and normal-appearing white matter (NAWM).

$K2_{BSW}$ showed no significant differences between tissue regions (P=0.557). Computer simulations confirmed the insufficient DSC sensitivity, as in every region the $K2_{BSW}$ values were below the derived limit of quantification ($4 \cdot 10^{-3}$ min^{-1}). In line with previous research[9,10], K_i was elevated in the WMH compared to GM and NAWM (P<0.001). $K2_{ATC}$ showed the opposite relation between the regions compared to K_i (P<0.001). Interestingly, the ATC scaling parameters were negatively related to the perfusion measures (P<0.001).

We conclude that DSC-MRI is not sensitive enough to measure subtle BBB leakage in cSVD. Using K2 as a direct measure for BBB leakage is not recommended in subtly leaking brain tissue until further research manages to better disentangle perfusion from leakage effects.

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