Comparison between MRI Blood-to-Brain Transfer Rate Constants from Individual MRI and Population Averaged Quantitative Autoradiographic Arterial Input Functions

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Introduction: An arterial input function (AIF), plasma concentration versus time curve, for an MR contrast agent (MRCA) is used to estimate the blood–brain barrier (BBB) permeability of microvessels and several other vascular related parameters. In dynamic contrast-enhanced MRI (DCE-MRI), an intravenous step-down infusion (SDI) procedure that maintains a constant gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA) blood concentration, has been shown to localize and quantify BBB opening more accurately than the bolus injection method commonly used.[1] The direct blood sampling technique employed by quantitative autoradiography (QAR) methods produces a better signal-to-noise ratio for determining the AIF than routine DCE-MRI methods. Furthermore, an acceptable AIF may not always be obtained using DCE-MRI. The present study investigates the possibility of using an average AIF (AIF_{avg}) obtained from a number of QAR experiments to estimate BBB permeability to Gd-DTPA for SDI procedure instead of using the individual MRI derived AIF (AIF_{ind}).

Methods: Male Wistar rats (~300 g; n = 5) were subjected to focal cerebral ischemia by suture occlusion of the right middle cerebral artery for 3 h followed by reperfusion via withdrawal of occluding suture. All MRI studies were performed at 7 Tesla. To localize and quantify the contrast enhancing areas, the blood-to-brain transfer constant (K^{trans}) for Gd-DTPA was estimated using Patlak plots under the conditions of BBB leakage with no reflux of MRCA during the MRI Look-Locker (LL) T_1-weighted data series.[1-3] The AIF_{ind}, acquired solely from MRI LL T_1 estimates, and AIF_{avg}, acquired from QAR using Gd-[^{14}C]DTPA as a tracer, were used to construct K^{trans}_{ind} and K^{trans}_{avg} maps, respectively. The QAR-AIF_{avg} was rescaled to match the MRI–AIF. Correlational analysis of the K^{trans}_{ind} and K^{trans}_{avg} values for the contrast enhancing regions-of-interest (ROI's) was performed and a paired t-test was used to compare the mean values. Pixel-by-pixel correlation of the clusters of K^{trans}_{ind} and K^{trans}_{avg} values for the ROI's was also analyzed using a generalized estimating equations (GEE) technique, using the R software package geepack.[4]

Results: Leaky ROI's for both the K^{trans}_{ind} and K^{trans}_{avg} maps as shown in Fig.1 were segmented based on an F-test statistic. In all cases, virtually identical areas of BBB opening were observed in both K^{trans}_{ind} and K^{trans}_{avg} maps. The comparison of mean K^{trans}_{ind} and K^{trans}_{avg} values from leakage ROI's yielded a high correlation (R=0.982, *P*=0.003) (Fig.2A). The GEE analysis was performed on 5 clusters corresponding to the 5 ROI's chosen, yielding a high correlation coefficient (R=0.952, *P*<0.0001). Pixel-by-pixel correlations for individual animals showed a range of R values (0.822-0.990). An example of pixel-by-pixel scatter plot from one rat is shown in Fig. 2B. The mean±SD of K^{trans}_{ind} and K^{trans}_{avg} values were $(3.13\pm0.84)\times10^{-3}$ min^{-1} and $(3.28\pm0.81)\times10^{-3}$ min^{-1}, respectively, and were not significantly different (*P*=0.101; two-tailed paired t-test). Thus, the K^{trans} values from both types of AIF's agreed closely with each other and were highly correlated.

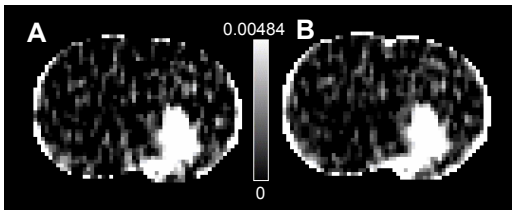

Fig.1. K^{trans}_{ind} (A) and K^{trans}_{avg} (B) maps of one animal. The scale bar between the maps indicates the range of K^{trans} values in min^{-1}.

Conclusion: Enhanced spatial resolution of areas with BBB opening was generally observed with the SDI technique. Both regression and GEE analysis of K^{trans}_{ind} and K^{trans}_{avg} yielded high correlations, suggesting that an averaged AIF for a given MRCA obtained from a standard technique such as QAR can be used in DCE-MRI to assess vascular permeability.

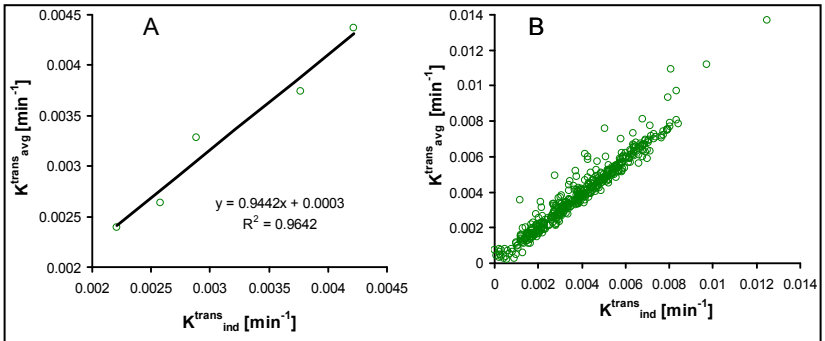

Fig.2. Scatter plots of mean K^{trans}_{ind} vs K^{trans}_{avg} values for all animals (A) and pixel-by-pixel K^{trans}_{ind} vs K^{trans}_{avg} values for one animal (B).

References

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