Verification of CSF-based HARM in Acute Stroke Patients with Early Blood-Brain Barrier Disruption

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Introduction

Evidence of HARM (Hyperintense Acute Reperfusion Marker) has recently been associated with hemorrhagic transformation and poor prognosis in acute stroke patients receiving intravenous rtPA.[1,2] Although it has been suggested that the location of HARM is in the CSF, the verification of CSF-based HARM versus involvement of the parenchymal space has yet to be performed. By calculating the ADCs for both CSF- and non-CSF suppressed DWI, as well as the apparent volume fraction of the parenchyma, the relative contributions of CSF and parenchyma to HARM enhancement may be determined.[3] We hypothesize that HARM regions will include areas with high ADCs and low parenchymal apparent volume fractions (i.e., CSF) in contrast to normal tissue.

Methods

A retrospective analysis of 10 acute stroke patients was performed. Data acquired pre- and post- Gd-contrast (FLAIR, FLAIR-DWI, standard DWI) within a 24-hour time period were analyzed. Regions with HARM on FLAIR (Fig.1B-C) were segmented following co-registration of all images. Additional volumes of interest (VOIs) were drawn for ischemic lesion and the comparable contralateral region (Fig.1F). ADC parameter maps (Fig.1G,1H) were calculated based on b = 0 and isotropic DW images for both FLAIR-DWI and standard DWI. Parameter maps for the apparent volume fraction of parenchyma (Fig.1I) were calculated based on the ratio of FLAIR-DWI (b = 0) to DWI (b = 0) images (Fig.1D,1E). Values for individual regions are expressed as mean (SD). Two-tailed paired t-tests were performed to assess differences between individual regions.

Results

HARM regions had significantly higher ADCs (1.6×10^{-3} mm^2s^{-1} (0.4)) than both ischemic stroke (0.74×10^{-3} mm^2s^{-1} (0.08), $p < 0.01$) and normal contralateral tissue (0.9×10^{-3} mm^2s^{-1} (0.2), $p < 0.01$), consistent with that of CSF. Although the ADCs in regions with HARM were slightly reduced from standard values (~3.0×10^{-3} mm^2s^{-1}), partial volume averaging of CSF and normal parenchyma is likely. Parenchymal apparent volume fractions for HARM regions, ischemic stroke, and contralateral tissue were (.40 (.10)), (0.74 (0.07)), and (0.76 (0.08)), respectively. Following volume fraction correction, ADCs in HARM regions were (2.7×10^{-3} mm^2s^{-1} (0.5)). Following CSF suppression, the ADCs for ischemic stroke and normal contralateral tissue were (0.63×10^{-3} mm^2s^{-1} (0.06)) and (0.79×10^{-3} mm^2s^{-1} (0.06)), consistent with previous reports.[3-5]

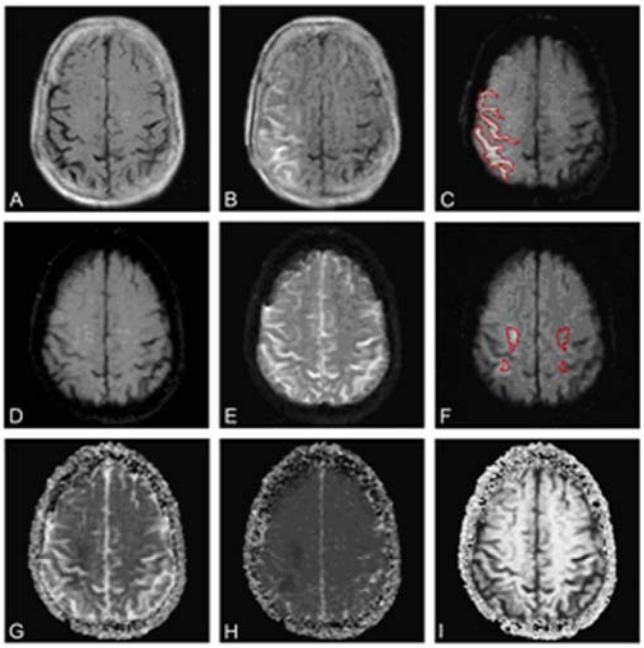

Figure 1. A) $FLAIR_{pre}$. **B)** $FLAIR_{post}$. **C)** $FLAIR\text{-}DWI_{post}$ with ROI delineation of HARM. **D)** $FLAIR\text{-}DWI_{pre}$ (b = 0). **E)** DWI_{pre}. **F)** $DWI\text{-}ISO_{pre}$ with ROI delineation of ischemic lesion and the comparable contralateral control. **G)** ADC. **H)** CSF-suppressed ADC. **I)** Volume Fraction of Parenchyma ($\lambda_{app\text{-}p}$).

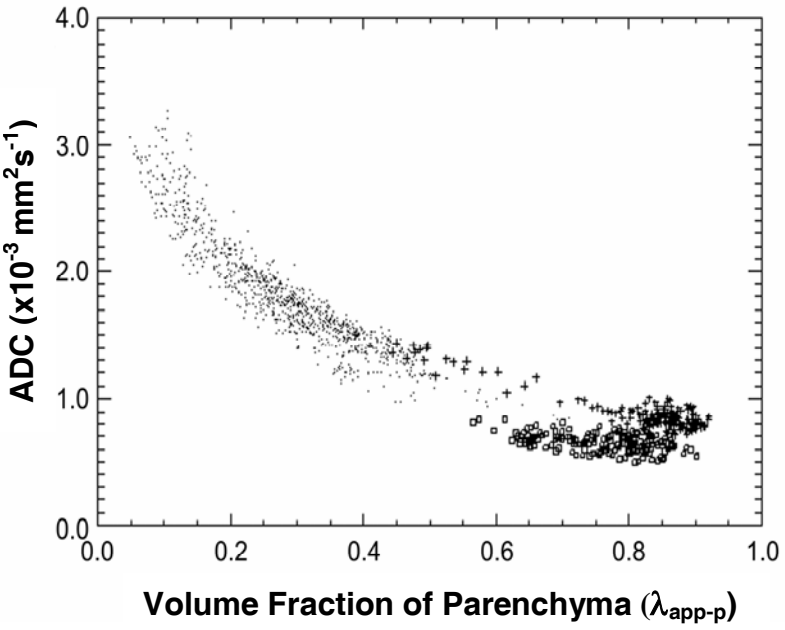

Figure 2. Scatterplot of ADC (non-CSF suppressed) versus volume fraction of parenchyma ($\lambda_{app\text{-}p}$) for HARM (dot), ischemic lesion (square), and contralateral tissue (plus). Note that HARM regions have a low $\lambda_{app\text{-}p}$ and high ADCs in comparison to ischemic stroke and normal tissue.

Conclusions

Regions with HARM included voxels with high ADCs and a low parenchymal apparent volume fraction in comparison to ischemic stroke and normal tissue. Based on these findings, HARM occurs predominantly in the CSF-space and not in the parenchyma. This may indicate leakage of the Gd-contrast from the vasculature into the CSF-space through a disrupted blood-CSF barrier and/or a disrupted blood-brain barrier.

References

[1] Latour LL et al. Ann Neurol 2004;56(4):468-477.

[2] Warach S, Latour LL. Stroke 2004;35(11 Suppl 1):2659-2661.

[3] Latour LL, Warach S. Magn Reson Med 2002;48(3):478-486.

[4] Falconer JC, Narayana PA. Magn Reson Med 1997;37(1):119-123.

[5] Hirsch JG et al. Magn Reson Imaging 1999;17(5):705-716.