Partial-Volume Effect on Ischemic Tissue-Fate Delineation using Quantitative Perfusion and Diffusion Imaging on a Rat Stroke Model

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Introduction Perfusion and diffusion imaging of animal stroke models in the acute phase remains limited to relatively low spatial resolution (64x64 matrix, 400x400x2000 microns) due to its high temporal-resolution requirements. Partial-volume effect at low resolution could hamper proper delineation of normal, ischemic and at-risk tissues by blurring the boundaries among different tissue types and tissue viability. Visual delineation of ischemic lesions by manually drawing ROI's on the diffusion- and perfusion-weighted images is a common clinical practice and the presence of PVE could lead to significant errors in identifying ischemic tissue fates. In addition, it is conceivable that a substantial number of pixels with mild apparent-diffusion-coefficient (ADC) or cerebral-blood-flow (CBF) reduction could arise simply from the physical effect of partial voluming, thereby confounding the interpretation of the operationally defined ischemic penumbra. High-resolution imaging could minimize tissue classification errors, increase pixel density leading to increased statistical power in pixel-by-pixel cluster analysis, and reduce signal loss due to intravoxel dephasing. The drawbacks are longer acquisition time and/or reduced signal-to-noise ratio (SNR).

In this study, the PVE on stroke imaging were systematically analyzed. Quantitative perfusion and diffusion imaging was performed at both high- and low-resolution in an experimental rat stroke model *during the acute phase*. PVE on the classification of ischemic tissue fates were quantitatively evaluated on a pixel-by-pixel basis. Analysis included the high resolution (HR, 128x128) data, low resolution (LR, 64x64) data, downgraded resolution data by taking the central 64x64 or 32x32 matrix from the high resolution (128x128) data, and zerofilled low-resolution data to achieve a higher nominal resolution.

Methods Fourteen male SD rats (300-350g,) were subjected to permanent MCAO. Rectal temperature, heart rate, respiration rate, and mean arterial blood pressure (MABP) were within normal physiological ranges. Two groups of animals were studied. In Group I (n = 6), **HR** data sets were acquired at 30, 60, 90, 120, and 180 mins post-occlusion followed by a LR data set (~ 200 mins). In Group II (n = 8), **LR** data sets were acquired at the same time points followed by a HR data set.

MRI was performed on a 4.7T magnet (Bruker). CBF was measured using the two-coil continuous arterial spin-labeling technique. HR data were acquired using 4-segment, EPI and LR data single-shot EPI. The MR parameters were FOV = 2.56cm x 2.56cm, TR = 2s/segment, b = 10, 1270s/mm^2, eight 1.5-mm slices, matrix = 128x128 for HR and 64x64 for LR, TE = 38ms for ADC and 15ms for CBF, 16 averages for ADC and 76 pairs for CBF.

An algorithm was developed to identify the normal-abnormal boundaries and ROI's were drawn (2-4 pixels thick) on the HR ADC and CBF maps. For comparisons, homologous ROI's were obtained by symmetrically reflecting the right-hemisphere ROI's along the midline to the left hemisphere. HR *versus* LR scatterplots and histograms were evaluated for the ADC and CBF data in the left and right hemispheres. Their distributions, means, standard deviations, FWHM were evaluated. PVE was analyzed for four data sets: *i)* 128x128 true matrix size, *ii)* 64x64 degraded from 128x128 data, *iii)* 32x32 degraded from 128x128 data, and *iv)* 64x64 degraded from 128x128 but then zero-filled to 128x128. Data are reported as mean ± SD.

Fig. 1

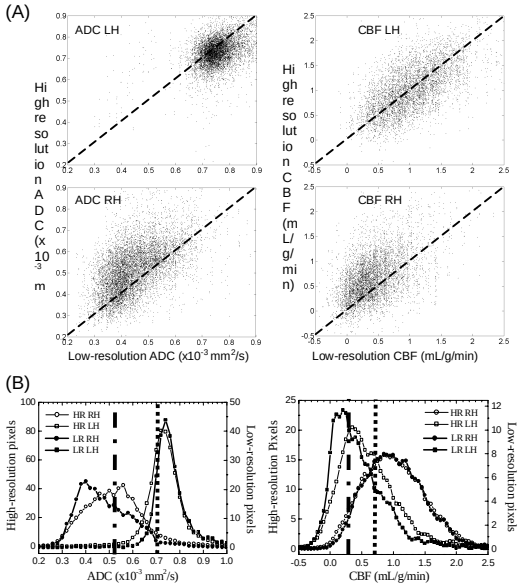
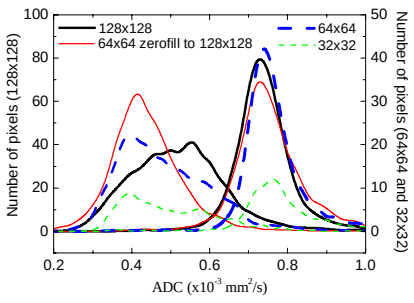


Fig. 2



Results & Discussions Visual inspection of the HR ADC and CBF maps showed clearer delineation of the border zones of different tissue types relative to the LR maps (not shown). **Figure 1A** shows the HR *vs* LR scatterplots (n = 14, 180 mins) from the ROI's along the normal-abnormal boundaries on the ADC and CBF maps. For each LR pixel, there are 4 HR pixels. In the absence of increased "noise", intrinsic tissue ADC or CBF heterogeneity and PVE due to ischemia *at HR*, all pixels on the scatterplots would fall onto the unity line. The dispersions about the unity line in the *left* hemisphere were indicative of reduced SNR and increased heterogeneity at HR. The ADC dispersions about the unity line were larger in the ischemic right-hemisphere relative to the left-hemisphere ADC. The right-hemisphere ADC dispersions were asymmetric about the unity line, the number of pixels located above the unity line was significantly larger than that under the unity line. These observations are indicative of the PVE *due to ischemia*. Surprisingly, CBF dispersions about the unity lines between the left and right hemisphere were comparable. This is because ischemia resulted in many pixels close to 0 mL/g/min, narrowing the distribution. Nonetheless, the number of right-hemisphere CBF pixels was also asymmetrically distributed about the unity line with more pixels located above than under the unity line, again indicative of the PVE *due to ischemia.*

ADC and CBF histograms for the HR and LR data at 180 mins post ischemia are shown in **Figure 1B**. In the left hemisphere, the ADC and CBF means, standard deviations, and FWHM were not statistically different between HR and LR data (P>0.05), despite reduced SNR and increased ADC and CBF heterogeneity at HR, likely compensated by the marked increase in the number of pixels at HR. The ADC-histogram of the right hemisphere was significantly wider than that of the left hemisphere. In the ischemic right hemisphere, the FWHM of the HR ADC distribution was slightly wider than that of the LR ADC distribution, and the peak of the HR distribution was located at a higher ADC. These observations suggested that HR imaging reduced PVE, and the effect of parcellating a single LR pixel into four HR pixels resulted in more "normal" or "close to normal" pixels, as indicated by the increased areas under curves at higher ADC.

With further reduction in spatial resolution (32x32), the right-hemisphere ADC distribution was similar to the 64x64 data set and its PVE was more severe than that of 64x64 (**Fig. 2**). The volume ratio of pixels below to above the ADC viability threshold (0.53 ± 0.02 x10^{-3} mm^2/s from Shen et al., JCBFM 2004) was 6.1, considerably larger than that at the 64x64 and 128x128 resolutions of 2.1 and 1.2, respectively. With zero-filling of the reconstructed 64x64 to 128x128, PVE was more severe relative to data without zero-filling, *i.e.*, biased to more core pixels at the expense of "at-risk" pixels. As controls, left-hemisphere ADC histograms were analyzed and found to be similar across four different effective resolutions.

Mis-classified pixels were quantified as ischemia progressed and ~30% of the total pixels was found to be mis-assigned due to PVE; majority of which were mis-assigned to abnormal pixels.

Conclusion: It was concluded that PVE: 1) misclassified substantial pixels along the *normal-abnormal* boundaries, 2) overestimated abnormal volumes at the expense of mostly "at-risk" and some "normal" tissues, 3) were more severe at the early time points post-ischemia, and 4) confounded the interpretation of the operationally defined ischemic penumbra. Zero-filling of low-resolution (64x64) data to 128x128 increased PVE.