Between-Scanner Variation in Normal White Matter ADC in the Setting of a Multi-Center Clinical Trial

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Introduction

The aims of this study are to determine whether a variety of clinical MRI scanner models produce consistent measures of brain white matter apparent diffusion coefficient (ADC), and to evaluate the scan-rescan variation in measured ADC between different scanner models. Data obtained in a multi-center clinical trial for treatment of gliobastoma multiforme (GBM) were used for this evaluation.

Assessment of the GBM treatment response traditionally relies on tumor size before and after therapeutic intervention. ADC maps calculated from diffusion weighted (DW) MRI, can provide information related to the microscopic cellular environment in solid tumors and may give an early indication of treatment response before size changes [1]. In order to use ADC imaging effectively in a multi-center chemotherapy clinical trial, it is necessary to evaluate the reproducibility of ADC data collected by multiple scanners in multiple centers.

Methods

Our pool data including 68 patients with GBM at six medical centers was used. The six scanners included two 3T scanner (Siemens TrioTim at two sites) and five 1.5T scanners (GE SIGNA HDx at two sites, GE SIGNA EXCITE, Siemens Avanto, Siemens Symphony). The protocol required use of the DW spin echo echo planar imaging technique using a b-factor between 700 and 1000 s/mm^2. All ADC maps were calculated from DW images with the same in-house software using a two-point method. Six patients had ADC with severe artifacts and five patients had abnormal normal white matter due to prior radiation. As a result, there were 57 patients with usable baseline scans. We only included scanners that scanned five or more patients, and furthermore, for the between-visit reproducibility study, we only included those patients who were scanned by the same scanner for at least two visits. As a result, we included 52 patients scanned by 7 scanner models for baseline variation study, and 40 patients scanned by 5 scanner models for the between-visit reproducibility study.

We used normal brain white matter (BWM) to evaluate ADC variation. A fixed size circular 2D region of interest (ROI) (r = 7 pixels) was manually placed on WM above the ventricles in ADC maps. ROI positioning was confirmed by board-certified neuroradiologist. We calculated the mean, median, and coefficient of variation (CV) of the ADC from each ROI. For the between-scanner variation study, we applied one-way ANOVA to compare the variation in baseline ADC mean, median and CV from the different scanners. For the scan-rescan variation study, we calculated the difference in the WM ADC measured in the same patient in two successive visits, and used one-way ANOVA to compare the between-visit variation among different scanners.
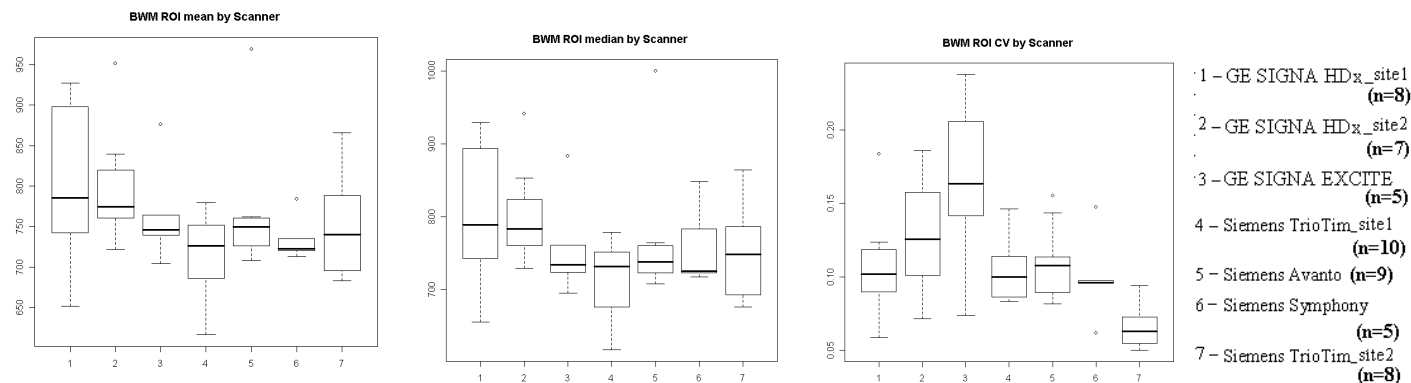
Results

Figure 1 shows the box plots of the baseline BWM ADC (units of 10^{-6} mm^2/s) mean, median and CV. The ANOVA test showed that there is no significant difference in mean (p=0.132) and median (p=0.199) between any two of the seven scanner models. However there is significant difference in CV (p=0.0005).
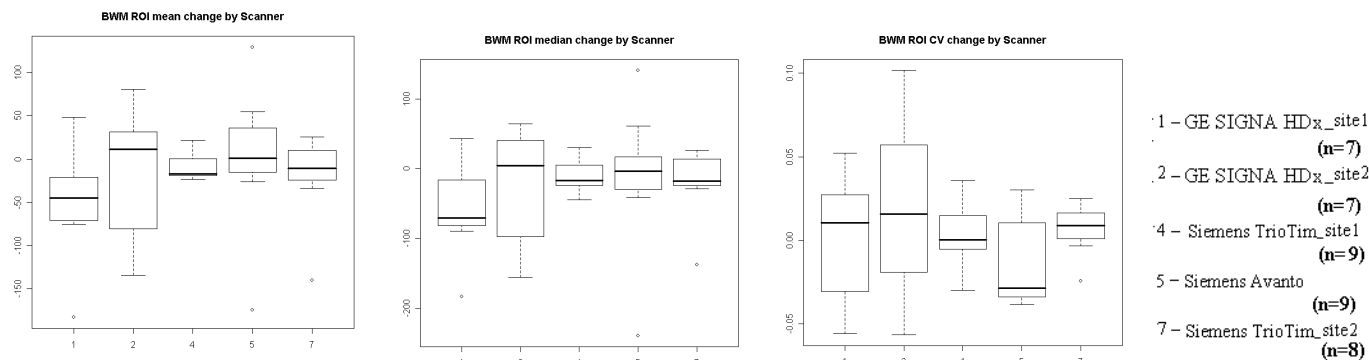

Figure 2 shows the box plots of the mean, median and CV difference in BWM ADC measured in two visits (5-7 weeks apart) from the same patient. The ANOVA test showed that there was no significant difference among the five scanners in mean change (p=0.551), median change (p=0.711), and CV change (p=0.395). A paired-t test on the aggregate data showed that there was not significant difference between baseline and follow up data in mean, median and CV (p>0.05). The intra-class correlation coefficient (ICC) was 0.57 for mean, 0.47 for median, and 0.54 for CV.

Conclusions

ADC reproducibility was assessed in the setting of multi-center clinical trial using BWM ROI analysis. Measured baseline BWM ADC values were consistent across six different scanner models from two manufacturers. Baseline CVs varied significantly between scanners, presumably due to image noise. The scanners showed no difference in their ability to reproduce BWM ADC measurement from the same patient on two successive visits. These latter data indicate that chemotherapy must produce changes of 50-100 10^{-6} mm^2/s to be considered significant.

Reference

[1] Chenevert TL, Stegman LD, Taylor JM, et al, J Natl Cancer Inst (Bethesda) 2000, 92:2029-36