Post-hoc spatial registration of multiple b-value diffusion weighted images improves test-retest reliability of ADC measurements in solid tumors in the body

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Background:
Accurate assessment of tissue apparent diffusion coefficient (ADC) requires acquisition and analysis of multiple b-value diffusion weighted images (DWI). One important source of variability in this ADC assessment is spatial misregistration across the multiple DWIs, particularly those at high b-values due to eddy current effects. The current work describes a simple post-hoc automated approach for spatial registration of multiple b-value DWIs. Applied to test-retest data set from a cohort of cancer patients, this approach enhanced repeatability of ADC measurements.

Methods:
DWI data was acquired in a cohort of 9 cancer patients as part of a phase 1 clinical trial protocol approved by local Institutional Review Boards (IRBs). Each patient was scanned twice within a week (median interval: 2 days, minimum/maximum: 1/6 days) prior to receiving any drug treatment. Each patient was scanned at one of three sites all using 1.5T Signa GE magnets with phased-array receive coils. DWI pulse sequences were all SE EPI. Scanning parameters were as follows: TR/TE=2865–4027/84.4–109.7 ms; FOV=380x380; matrix=256x256; 20–22 slices; slice thickness=5 mm, 8 averages, free breathing. One of the following two sets of b-values was used with each patient: (1) 0, 10, 30, 50, 100, 650, 1000 s/mm^2, or (2) 0, 10, 100, 500, 850 s/mm^2. Only the three DWIs from either set with b-values ≥ 100 s/mm^2 were used for estimation of ADC parametric maps under the assumption of monoexponential decay model. Data processing and analyses was all done with Matlab (Mathworks) software developed in-house. Regions of interest (ROIs) were manually defined for tumor, and ROI-based mean, median, 25th and 75th percentile ADC values used for test-retest reliability analyses. A total of 11 tumors were tested and test-retest reliability was assessed by Bland-Altman and scatter plots, intraclass correlation coefficient (ICC), coefficient of determination (R^2) and coefficient of variation (CoV). DWI spatial registration was accomplished for each ROI as follows. Using the DWI at b=100 s/mm^2 as reference, higher b-value DWIs were iteratively shifted on x- and y-axes directions so as to minimize the sum-of-squared-differences between measured and estimated DWIs within each ROI. Test-retest reliability parameters were recalculated for co-registered data sets.

Results and conclusions:
Figure 1 shows an example of DWIs from a single patient examination and the effectiveness of the spatial registration algorithm proposed in this work. Figure 2 shows overlaid Bland-Altman plots for ADC measured in the original and co-registered. Table 1 shows the test-retest parameter results for original and co-registered data. Overall, consistent with previous reports on ADC measurement repeatability (Koh et al 2009) there was good test-retest repeatability of ROI-based ADC measurements in both original and co-registered data as assessed by ICC, CoV and R^2. Albeit slightly, both CoVs and R^2 were systematically smaller and ICC systematically larger in co-registered than in original data suggesting ADC measurements were more reliable in co-registered data. Future work will focus on ROI-based ADC measurements with co-registered DWIs and its sensitivity to therapeutic intervention.

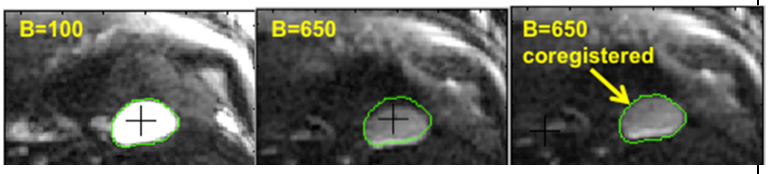

Figure 1: Example of DWI misregistration (left and center panels) and effectiveness of post-hoc registration procedure (left and right panels). Yellow outlines are ROIs defined on B=100 s/mm^2 DWIs.

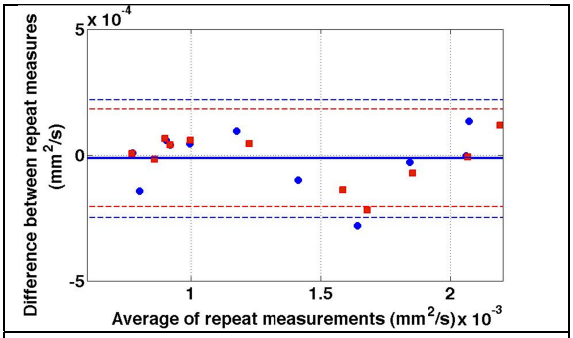

Figure 2: Bland-Altman plots for original data (blue) and co-registered data (red). Solid lines depicts mean difference between repeat measures. Dashed lines are limits of agreement.

	Original Data			Co-registered Data		
Endpoint	CoV	R^2	ICC (CI)	CoV	R^2	ICC (CI)
Mean	9.9%	0.92	0.96 (0.86 0.99)	8.1%	0.95	0.97 (0.91 0.99)
Median	8.7%	0.94	0.97 (0.91 0.99)	6.9%	0.98	0.98 (0.94 1.00)
25th Perc	11.1%	0.92	0.96 (0.86 0.98)	10.3%	0.93	0.97 (0.88 0.99)
75th Perc	10.1%	0.91	0.96 (0.86 0.99)	7.0%	0.96	0.98 (0.93 0.99)

Table 1: Summary test-retest statistics for original and co-registered ADC data. N=11. All coefficients of determination, R^2, were statistically significant at p<0.0001.

References: Koh et al. *Eur Radiol* (2009) 19: 2728–2738