**Quantitative Imaging Network Demonstration of ADC Nonlinearity Bias in Multi-center Trials**

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**Introduction**

To establish confidence levels for quantitative diffusion weighted imaging (DWI) that uses the apparent diffusion coefficient (ADC) as a radiological marker [1], the sources of instrumental bias need to be identified and mitigated [2]. Evaluation of bias correction for ADC mapping [3,4] requires independent characterization of MR system bias. Here, a uniform protocol to characterize system-specific bias was implemented across different MRI platforms utilized in multi-center clinical trials. The proposed protocol allows measurement and evaluation of relative contributions to ADC bias from different instrumental settings, such as, gradient nonlinearity, shim imperfections and cross-terms with imaging gradients.

**Methods**

DWI measurements were performed using a long-tube (260x29mm) ice-water phantom [2,3], in which a tube of distilled water is submerged in an ice-water bath. A platform was built to ensure controllable phantom elevation in the magnet bore, which was adjustable to +/-10mm from isocenter. The phantom was scanned using X,Y, and Z diffusion gradients individually at three offset positions from isocenter (0 and +/-70mm) for two orientations (superior-inferior, SI, and right-left, RL). The ADC was measured from a 1cm circular ROI placed in the water tube at 30-40 offset values for each phantom position. The unidirectional nonlinearity bias was estimated as a ratio of the measured to the known ice-water ADC value [2]. The relative contribution of shim error was evaluated from the apparent versus known ROI elevation, while cross-terms with the imaging gradients were detected from the ADC shift near isocenter for the DWI gradient applied along the slice direction.

**Results**

The DWI acquisition protocol was implemented by seven quantitative imaging network (QIN) centers utilizing nine MRI systems from three vendors (Siemens, Philips, GE). The collected DICOM data was uploaded for analysis by a single center. The acquired stack of slices from all phantom offsets provided a spatial extent of approximately +/-150mm with about 50 non-overlapping ADC measurements along the SI and RL axes for each of the three diffusion directions (Fig.1). All MRI platforms exhibited ADC map bias in excess of the measurement error for ROI offsets from the isocenter greater than 40-50mm. The observed nearly parabolic and symmetric dependence on ROI offset (Fig.1) for unidirectional bias was consistent with gradient nonlinearity characteristics [2,3]. The largest (negative) bias (> 20%) was observed along SI for X- and Y-gradients. For off-center measurements, the gradient nonlinearity bias accounted for the bulk of observed ADC error. Shim imperfections appeared to produce bias asymmetry for some systems, while imaging cross-terms contributed a small (< 3%) offset-independent bias only for diffusion gradient along the slice direction.

**Conclusion**

The implemented protocol for multi-scanner bias evaluation provides a useful solution for empiric description of potential instrumental bias in multi-center clinical trials. Separate assessment of bias is conducted for each MRI gradient coil. The performed measurements confirm gradient nonlinearity as a significant source of ADC map bias on clinical scanners independent of vendor platform with minor contributions of both shim and imaging cross-terms. The extent of bias is dependent on gradient coil design and diffusion gradient direction.