Published in final edited form as:

J Magn Reson Imaging. 2018 December ; 48(6): 1498–1507. doi:10.1002/jmri.26201.

Improving Apparent Diffusion Coefficient Accuracy on a Compact 3T MRI Scanner using Gradient Non-linearity Correction

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Abstract

BACKGROUND—Gradient non-linearity (GNL) leads to biased apparent diffusion coefficients (ADCs) in diffusion weighted imaging. A gradient non-linearity correction (GNLC) method has been developed for whole body systems, but yet to be tested for the new compact 3T (C3T) scanner which exhibits more complex GNL due to its asymmetrical design.

PURPOSE—To assess the improvement of ADC quantification with GNLC for the C3T scanner.

STUDY TYPE—Phantom measurements and retrospective analysis of patient data.

PHANTOM/SUBJECTS—A diffusion quality control phantom with vials containing 0-30% polyvinylpyrrolidone in water was used. For in-vivo data, 12 patient exams were analyzed (median age =33).

FIELD STRENGTH/SEQUENCE—Imaging was performed on the C3T and two commercial 3T scanners. A clinical DWI (TR = 10000 ms, TE = min, b = 1000 s/mm²) sequence was used for phantom imaging and 10 patient cases and a clinical DTI (TR = 6000-10000 ms, TE = min, b = 1000s/mm²) sequence was used for two patient cases.

ASSESSMENT—The 0% vial was measured along three orthogonal axes, and at two different temperatures. The ADC for each concentration was compared between the C3T and two whole body scanners. Cerebrospinal fluid and white matter ADCs were quantified for patient and compared to values in literature.

STATISTICAL TEST—Paired t-test and two-way ANOVA

RESULTS—For all PVP concentrations, the corrected ADC was within 2.5% of the reference ADC. On average, the ADC of cerebrospinal fluid and white matter post-GNLC were within 1% and 6% of values reported in literature respectively and were significantly different from the uncorrected data (p<0.05).

DATA CONCLUSION—This study demonstrated that GNL effects were more severe for the C3T due to the asymmetric gradient design, but our implementation of a GNLC compensated for these effects, resulting in ADC values that are in good agreement with values from literature.

Keywords

Diffusion weighted imaging; gradient non-linearity; apparent diffusion coefficient

INTRODUCTION

Gradient linearity is essential for accurate spatial localization in MRI, as uncorrected gradient non-linearity (GNL) leads to unwanted image blurring and distortion (1–3). While commercial MR scanners have some degree of gradient non-linearity or non-uniformity due to engineering limitations, manufacturers commonly employ an image-based post-processing GNL correction algorithm (e.g., “gradwarp” on GE’s system) to compensate for spatial encoding distortions (1). This standard correction, however, does not correct the diffusion measurement bias caused by non-linear diffusion-encoding gradients, which results in a spatially-dependent error in quantitative diffusion-weighted imaging (DWI) (4, 5). In a system with perfectly linear gradients, the apparent diffusion coefficient (ADC) can be estimated using images acquired with distinct b-values. The b-value is dependent on the duration and amplitude of the diffusion encoding gradient pulses in addition to the time interval between the two gradient pulses. Instead of a uniform b-value for all spatial locations, the gradient nonlinearity property requires description of the spatial-dependent b-value matrix, which is not trivial to determine. In this case, the gradient field map tensor and the idealized gradient vector can be used to approximate the b-value matrix (4, 6). The gradient field map tensor can be generally expressed using spherical harmonic polynomial expansion (7, 8). The model coefficients can be obtained using electromagnetic (EM) simulation or phantom calibration (1, 9, 10). In general, for conventional whole-body systems, only model coefficients of odd-orders (e.g., 3rd order, 5th order, etc.) are required for distortion correction when imaging the head. A more detailed discussion of this GNLC method has been described in Bammer et al and in Tan et al. (4, 6).

In addition to the standard GNL correction for image geometric distortion, the effects from non-linear gradients in diffusion-encoding can also be corrected in diffusion tensor imaging (DTI) and diffusion-weighted imaging (DWI) (4–6). It has been shown that the application of retrospective gradient nonlinearity correction (GNLC) can reduce the GNL-related errors and differences in ADC between different scanners from 10% to 2% (4, 6). The effects from GNLC as applied to a multicenter trial for quantitative breast DWI was shown to reduce errors in ADC maps by up to 12% (11).

A novel, compact 3T MR scanner (C3T) (12, 13) was developed as a technology demonstrator under an NIH-funded program. The motivation behind the C3T was to demonstrate the advantages offered by a lightweight, low-cost, and high-performance MR system. The C3T was designed with a high-performance gradient system with a 42 cm inner diameter. Due to its relatively small size, the gradient system can achieve 80 mT/m amplitude and 700 T/m/s slew rate simultaneously, while remaining below the peripheral

nerve stimulation limit (12–14). To facilitate patient access, it was necessary to shift the imaging volume towards the patient end of the bore to accommodate both the head and shoulder. This shift is accomplished by using asymmetric gradient coil windings (12, 14, 15) along the bore axis (i.e., the physical Z axis) for both transverse gradients (i.e., the physical X and Y axes). The asymmetric configuration allows the homogeneous gradient volume to be closer to the patient end of the bore. However, this asymmetry introduces more complicated GNL compared to the conventional symmetrical systems that are used in the whole-body scanners. Therefore, both odd- and even- order spherical harmonic polynomials, up to the 10th order, are required to accurately model the gradient field map (10).

While GNLC algorithms for diffusion have been demonstrated successfully on conventional whole-body MR scanners equipped with symmetrical gradient systems, they have yet to be tested asymmetric gradient systems, except in our preliminary report (16).

The purpose of this work was to investigate the quantitative accuracy and precision of the ADC on the C3T using the GNLC algorithm with these higher-order coefficients, and to determine how they compare to whole-body scanners.

MATERIALS AND METHODS

Phantom Study/Preparation

A diffusion quality control (QC) phantom (HPD Devices, Boulder, CO) was selected for our phantom study as it met the recommendations of an ideal phantom for diffusion quantification as set out by Keenen et al. (17). This commercial phantom was also based on the design originally developed by Boss et al. (18). The phantom consisted of 13 vials of 3 cm diameter and filled with varying concentrations of polyvinylpyrrolidone (PVP) in water contained within a 19.4 cm diameter plastic sphere (18, 19). The vials in the phantom were arranged in two concentric rings. Vials in the inner and outer rings were spaced 4 cm and 6.5 cm apart respectively with PVP concentration ranging from 0-50% with a 10% increment clockwise. There was one additional 0% PVP vial in the center. The phantom was imaged in four orientations: the standard, axial position with the long axis of the vials parallel with the bore axis (physical z-axis) direction, and rotated about the z-axis every 90° to measure the ADC of each PVP concentration in various quadrants of the axial field of view (FOV). In addition, the phantom was imaged at two different temperatures: 0°C (reference standard from the literature) and at ambient room temperature (to measure ADC values as obtained in a clinical environment). Following recommendations by the phantom manufacturer, the phantom was prepared with an ice-water bath approximately 2 hours prior to imaging, and additional ice was added immediately beforehand to ensure a stable 0°C temperature for the duration of the imaging session. For higher temperature imaging, the phantom was filled with deionized water and was equilibrated to ambient room temperature (20°C) in each scanner room overnight before imaging. The phantom temperature was verified with a thermometer to within $\pm 0.05^\circ\text{C}$ prior to and after each imaging session.

DWI was performed with the same phantom on three different MR scanners using an 8-channel head coil (Invivo, Gainesville FL) for cross-platform comparison. The same brain coil was used for volunteer experiments. The three scanners include a C3T scanner, a

Discovery MR750w whole-body, 70 cm bore scanner (GE Healthcare, Waukesha, WI) and a Signa HDxt 3T whole-body, 60 cm bore TwinSpeed scanner using zoom mode gradient (GE Healthcare, Waukesha, WI).

MRI Acquisition

Images were acquired with a clinically used axial brain DWI protocol with a single-shot, spin-echo echo planar imaging sequence with three orthogonal (X,Y,Z) diffusion gradient directions. The imaging parameters were: b-values = 0, 1000 s/mm², TR = 10000 ms, slice thickness = 4 mm skip 0, FOV = 22 cm × 22 cm, number of slices = 10, imaging matrix: 128×256, number of signal averages (NEX) = 1, and parallel imaging acceleration factor (ASSET) R=2 which is GE's implementation of sensitivity encoding (SENSE) (20). Three-dimensional “gradwarp” correction for only spatial encoding distortion in the source images was enabled for the C3T and MR750w, while the software version on the Signa HDxt was limited to two-dimensional “gradwarp” correction. The acquisitions on the C3T employed both real-time gradient pre-emphasis and frequency shifting to compensate for additional concomitant field terms due to the asymmetric gradient design (21, 22).

GNLC Theory

Assuming a linear gradient system, the ADC can be estimated using Eqn. 1, where $S(b)$ is the signal with b-value (s/mm²), b and $S(0)$ is the signal when $b = 0$ s/mm².

$$\ln\left(\frac{S(b)}{S(0)}\right) = -b \cdot ADC \quad (1)$$

However, as described in the introduction, the gradient nonlinearity property requires spatial-dependent b-values denoted with a b-matrix but is not trivial to determine. The gradient field map tensor $\Lambda = [\Lambda_x \ \Lambda_y \ \Lambda_z]$ and idealized gradient vector $g = [g_x \ g_y \ g_z]^T$ can be used estimate the b matrix to account for the gradient nonlinearity as given in Eqn. 3

$$\ln\left(\frac{S(b)}{S(0)}\right) = -bg^T \Lambda^T ADC \Lambda g \quad (2)$$

Spherical harmonic polynomials were used to characterize the gradient field map tensor. Both odd- and even model coefficients up to the 10th order (i.e., 10th degree) were initialized with values from EM simulation and minimized with an iterative calibration procedure. The EM simulation derived coefficients were verified in Tao et al. (10) using known fiducial locations from an Alzheimer's Disease Neuroimaging Initiative (ADNI) phantom. The ADNI phantom consisted of 160 fiducial markers spanning a 20 cm diameter spherical shell. In order to accurately characterize the full 26 cm diameter of spherical volume of the gradient system, the phantom was imaged at isocenter and also at ± 3 cm in each of the three orthogonal directions (10). The estimates of the fiducial locations were determined with the model coefficients and the fiducial locations identified within the images. The mean square error between the initial estimate and the true location of the fiducials represented the residual gradient nonlinearity. The coefficients were then optimized with Gauss Newton

iteration as presented by Trzasko et al. to minimize the root mean square error between the true and estimated fiducial locations (24). This methodology has been discussed in detail in Tao et al. (10).

The GNLC using EM simulation derived coefficients was retrospectively applied to all source images using the electromagnetic simulation-determined spherical harmonic coefficients to compute the b-value corrected diffusion weighted images (6, 23). ADC maps were calculated from the diffusion-weighted images with and without GNL correction using built-in vendor provided software.

C3T Phantom Data Analysis

The three vials with 0% PVP were used to investigate the effect of GNLC for various regions in the FOV and temperature settings. The three vials were referred to as the center (isocenter), inner (4 cm to isocenter) and outer vials (8 cm to isocenter). The mean ADC for each vial was determined in a circular region-of-interest (ROI) with 2 cm diameter positioned in the cross-section of each vial for all slices. First, the mean ADC of the center 0% vial was measured along the slice direction (z-gradient) ranging from -2.2 mm to 1.4 mm relative to isocenter (inferior-to-superior direction). Second, the mean ADC was measured as a function of radial distance from isocenter. The ADC from each vial was averaged over the two central slices about isocenter. Third, the mean ADC was measured as a function of rotation angle (every 90°) at a fixed radial distance (+8 cm) from isocenter and also averaged over the two central slices. Lastly, the effect on temperature was measured for all ROIs of the center 0% PVP vial in the two central slices. The ADC for water established in literature at 0°C and 20°C were $1.12 \times 10^{-3} \text{ mm}^2/\text{s}$ and $2.023 \times 10^{-3} \text{ mm}^2/\text{s}$ respectively and was used as the assumed ground truth ADC (25–28).

Inter-scanner Analysis

The mean ADC for each PVP concentration from each scanner was calculated by averaging over all ROIs, for all 10 slices and all orientations at 0°C. PVP concentrations greater than 30% were omitted for the inter-scanner analysis because imaging parameters were not optimized for lower diffusivity materials. The reference ADC values for the inter-scanner analysis were obtained from a multi-center study (28) using a similar phantom with the same PVP concentrations.

In-vivo Experiments

In addition to our phantom study, a group of healthy volunteer subjects ($n = 10$ DWI and $n = 2$ DTI) were imaged on the C3T system using an IRB-approved protocol. Written informed consent was obtained from all subjects. The images were processed and analyzed retrospectively to demonstrate the in vivo improvement in ADC accuracy with GNL correction. Two separate analyses were performed with the default calculated ADCs and GNL corrected ADCs for cerebrospinal fluid (CSF) and white matter (WM). First, the ADCs from all patient cases ($n = 8$ females, $n = 4$ males, age range = 18-62, median age = 33) were compared as a function of distance of the ROIs relative to isocenter. Second, the mean diffusivity (MD) was compared between DTI scans for one volunteer (30 y.o. male) imaged on both the C3T scanner and a whole body scanner (GE MR750w).

The imaging parameters for the clinical DWI protocol were: $b = 1000 \text{ s/mm}^2$ FOV: $24 \text{ cm} \times 24 \text{ cm}$, slice thickness = 4 mm with a 4 mm gap, TR = 10000 ms, TE = minimum (44.3-57 ms), number of slices = 36-40, imaging matrix: 128×256 , number of averages = 1, and parallel imaging acceleration factor: $R = 2$ (using sensitivity encoding). ADC maps were generated with DWI data before and after GNL correction. For the DTI cases, two adult volunteers were scanned with a clinical brain diffusion tensor imaging (DTI) protocol. The imaging parameters were: FOV: $24 \text{ cm} \times 24 \text{ cm}$, slice thickness: 2.5 mm with 2.5 mm gap between slices/4 mm with 4 mm gap between slices, TR = 6000 ms/8000 ms, TE = minimum (59.3-85.4 ms), imaging matrix: 96×96 , parallel imaging acceleration factor: $R = 2$, 10 diffusion-encoding directions and b-value: 0, 1000 s/mm^2 . MD maps were generated from both the standard DTI, and the GNL corrected DTI data.

Four regions of interest were selected in the CSF, two corresponding to the left (ROI 1) and right (ROI 2) middle ventricles and two regions in the left (ROI 3) and right (ROI 4) subarachnoid space near the superior region of the imaging volume. Four regions were also selected in the WM, left (ROI 1) and right (ROI 2) regions near the ventricles and left (ROI 3) and right (ROI 4) regions in the WM of the frontal lobe. DWI and DTI ROIs were selected with a nominal area of 50 pixels and 20 pixels due to differences in pixel size.

Statistical Analysis

A paired t-test was used to determine if there was a difference in ADC of the 0% PVP vial among the different locations measured to the reference ADC and if there was a significant difference between the patient ROIs for CSF and WM to the mean ADC reported by Helenius et al. (29). P-values were calculated before and after GNLC and the null-hypothesis was there is no difference in ADC for our sample set compared to the corresponding reference ADC. A paired ttest was also used to establish if there was a significant difference between the GNLC and non-GNLC ADC for each of the main conditions investigated. Finally, two-way ANOVA analysis was performed to determine the inter-scanner agreement.

RESULTS

C3T Analysis

An example ADC map for the central axial slice in the phantom at 0° rotation angle from the C3T scanner is shown in Fig. 1. The mean ADCs for each configuration are summarized in Fig. 2. In the superior/inferior (S/I) direction (where negative distances correspond to the inferior direction relative to isocenter), there was an overall improvement in the mean ADC along the slices resulting in a $<1\%$ difference from the reference value. No significant difference was observed between the inferior and superior end of the phantom with a coefficient of variation of $<1\%$ over the range of slices analyzed both before and after correction ($p > 0.05$) (Fig. 2a). However, a distinct relationship between the ADC and radial distance was observed prior to GNLC. The outer vial had the greatest difference from the reference value with a 7% increase in ADC with a mean ADC of $(1.16 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s}$ between the three radial locations from isocenter. Post correction, ADC values of all vials were corrected to a value much closer to the reference value with a mean of (1.12 ± 0.02)

$\times 10^{-3} \text{ mm}^2/\text{s}$ (Fig. 2b). This correction resulted in similar ADC values for different radial distances. The mean ADC of the outer vial for four rotated positions was $(1.19 \pm 0.05) \times 10^{-3} \text{ mm}^2/\text{s}$ and $(1.12 \pm 0.04) \times 10^{-3} \text{ mm}^2/\text{s}$ before and after GNLC respectively, resulting in a mean ADC change of 7% and was within agreement of the reference ADC (Fig. 2c). Using ROIs from all locations for our statistical test, a significant difference between the ADC before GNLC and the reference ADC was observed with p-value 0.0005, but after GNLC the p-value was 0.8 indicating our null hypothesis could not be rejected. The paired t-test performed on the GNLC and non-GNLC data resulted in a p-value of 0.002. At two different temperatures, the mean ADC for ROIs of all 0% PVP vials were $(1.19 \pm 0.02) \times 10^{-3} \text{ mm}^2/\text{s}$ and $(2.04 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s}$ post-correction at 0°C and 20°C respectively (Fig. 2d). The corrected mean ADC matched the reference value at 0°C and was within 1% of the reference value at 20°C post-correction. Overall, the GNL correction provided more uniform estimates of ADC regardless of location and for temperatures that were measured.

Inter-scanner Analysis

A summary of the mean ADC for 0-30% PVP is presented in Fig. 3. A downward shift towards the assumed ADC was observed for all scanners except the MR750w at the 30% PVP concentration. Prior to GNLC, the difference between the ADCs from all vials and the reference values ranged between 3.6-6.1%, 1-5.8% and 3.8-5.2% for the C3T, MR750 and Signa HDxt scanners, respectively. Post correction, the difference from the reference ADC was reduced to be between 0.6-1.3%, 1-1.3%, and 0.4-2.3% respectively for the three scanners. In addition, the change in coefficient of variation (COV) post-correction was greatest for 0% PVP vial on the C3T (2.9% to 0.8%); the COV ranged between 1.3%-2.9% before correction and 0.8%-1.5% after GNLC for all scanners. COV was 2-3.5% for 10% PVP and 3.1-3.7% for 20% PVP but with GNLC was improved to 0.9-1.5% and 2-3.2% respectively. At 30% PVP, COV improved from 3.5-3.7% to 2.1-3% for the other two scanners except for Signa HDxt where the COV increased from 3.1% to 3.2%. The overall trend showed a decrease in the ADC post-GNLC with a larger decrease in the standard deviation for lower PVP concentrations. A two-way ANOVA analysis returned a p-value of 0.007 before GNLC and 0.1 post-correction, indicating interscanner agreement improved such that the null hypothesis could no longer be rejected.

In vivo experiment

The reference mean ADC used for analysis for CSF and WM were $(3.02 \pm 0.16) \times 10^{-3} \text{ mm}^2/\text{s}$ and $(0.7 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s}$ respectively as shown in Fig. 4 (29). Figs. 4a) and 4c) show the ADC before correction for CSF and WM respectively with the GNL corrected ADC in Figs. 4b) and 4d). Decreasing ADC was observed with increasing distance from isocenter in the patient superior direction. The mean ADC for CSF and WM for our 12 patient cases were $(2.90 \pm 0.26) \times 10^{-3} \text{ mm}^2/\text{s}$ and $(0.70 \pm 0.05) \times 10^{-3} \text{ mm}^2/\text{s}$ before correction with p-value 0.0002 and 0.07 and $(3.01 \pm 0.11) \times 10^{-3} \text{ mm}^2/\text{s}$ and $(0.74 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s}$ with p-value 0.2 and 0.0001 respectively after GNLC. Furthermore, the measured uniformity across all ROIs and cases was 81% and 82% for CSF and WM before correction but improved to 93% and 92% after GNLC. Our results show that GNLC is able to correct for disparities in ADC quantification regardless of location from isocenter and trends towards a more uniform ADC (decrease in variance). A paired t-test resulted in a p-value < 0.0004 for

both CSF and WM indicating a significant difference between the mean ADC before and after GNLC correction.

Fig. 5 shows two example MD slices of the axial brain DTI from one volunteer. ROIs were not explicitly shown due to the small size relative to the image. The difference ratio map shows the bias is mainly located in the periphery of the FOV for the axial slice near isocenter and across the full imaging area for the slice away from isocenter which is due to increased non-linearity effects as distance from isocenter increases in both the radial and S/I direction, and correlates well with the decreased ADC observed in regions furthest from isocenter.

Fig. 6 summarizes the effect of GNL correction on the ADC for a whole body scanner versus the C3T from the same volunteer. The figure shows the mean ADC as a function of different ROIs rather than axial distance from isocenter to better illustrate the change in ADC. ROIs 1 and 2 correspond to 5.8 cm and 1.6 cm from isocenter and ROIs 3 and 4 correspond to 9 cm and 4.8 cm from isocenter both along the slice direction for the MR750w and C3T respectively. ADC values for CSF measured at 4.8 cm from isocenter were approximately 9% lower and 7% lower for WM as compared to ADC values measured at 9 cm from isocenter. In addition, for similar distances from isocenter, the measured ADC for the C3T was slightly underestimated compared to the MR750w. Overall, the GNLC patient data showed greater improvement in the mean ADC maps for regions further from isocenter and both CSF and WM agreed with values observed in literature.

DISCUSSION

From our observations, ROIs of vials located farther from isocenter in the axial plane had larger ADC bias from the reference value as compared to ROIs displaced from isocenter in the slice direction. Reduced bias was observed in the slice direction because the length of the vials limited ADC quantification from -2.2 cm to 1.4 cm from isocenter, whereas ADC quantification in the axial plane was measured up to 8 cm radially from isocenter. Non-uniform bias was observed when the phantom was rotated every 90° indicating the magnetic field was not symmetric but our results show appropriate gradient modelling can account for this. The observed ADC of water at 0°C in our study was $(1.12 \pm 0.01) \times 10^{-3} \text{ mm}^2/\text{s}$ and is consistent with the ADCs reported by Palacios et al. (28), Easteal et al. (26), Jerome et al. (30), and Hectors et al. (31). However, our observed ADC was slightly larger than the ADC established by Holz et al. (25) and Chenevert et al. (32) but was not statistically different. At 20°C, our mean ADC $((2.04 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s})$ for water was within 1% of the assumed ground truth ADC $(2.023 \times 10^{-3} \text{ mm}^2/\text{s})$ (25–27). The mean ADCs for various PVP concentrations at 0°C were very similar to results published in literature (within 2%) except for vials with PVP concentration $\geq 30\%$. This was due to a sub-optimal imaging protocol for higher PVP concentration vials that have lower diffusivity values that are not well-matched to the b-value used in this study (28, 30, 31). Studies have shown that the number of b-values, the selected b-values and other scan parameters such as TE affect the overall ADC estimate, particularly for low diffusivity materials (33–35). Our study used a clinical DWI protocol with b-values of 0 and 1000 mm^2/s , whereas the reference protocol used diffusion tensor imaging with 4 b-values and a maximum b-value of 1300 mm^2/s . The

protocol used in this work was optimized for ADC values observed in a typical brain imaging study which was adopted to evaluate the effect of GNL and its correction in clinical applications; therefore, imprecise ADC estimates were expected for low diffusivity vials. This effect was apparent as the ADC accuracy decreased and PVP concentration increased.

Our results from the C3T showed slightly greater improvement with the GNL correction compared to the whole-body systems when quantifying a range of PVP concentrations. There are two possible reasons that may contribute to this finding. First, real time field adjustment (RTFA) (36) for correcting higher-order eddy current effects was available in the C3T and the MR750 whole-body but not in the HDx whole-body. Second, potentially more accurate field maps in the form of higher-order basis functions were used to characterize the C3T system; up to 10th-order spherical harmonic polynomial terms were used for the C3T (10) while up to 5th-order terms (default configuration provided by manufacturer) were used for the whole-body systems. With symmetric gradients in whole-body systems and an overall larger bore, higher order terms would not be expected to substantially improve clinical diffusion imaging for a head-sized field of view. However, a study by Tan et al. showed that modeling conventional whole body scanners up to the 7th order increased ADC accuracy by 1% as compared to the traditional 5th order modeling (6) which could provide improved agreement in ADC measurements between scanners.

While the absolute ADC value of the CSF in individuals can vary, it is expected that ADC values should be fairly uniform and consistent for the same subject. It is further expected that the CSF should exhibit similar if not the same ADC values throughout the entire brain volume since it mostly consists of water and its structure does not change in different regions of the brain. Interestingly, the estimated ADC for CSF in the patient example corresponded well with the values from a study by Helenius et al. (29). The mean CSF ADC (from the left and right middle ventricle) for a group of 40 healthy individuals was reported to be $(3.02 \pm 0.16) \times 10^{-3} \text{ mm}^2/\text{s}$ compared to our corrected ADC of $(2.9 \pm 0.2) \times 10^{-3} \text{ mm}^2/\text{s}$ (p value = 0.2) averaged over the four selected ROIs. ROIs 1 and 2 were already similar to the ADC value observed by Helenius et al. due to the proximity of the ventricles to isocenter, but ROIs from the superior slice had a much more significant change in the mean ADC from gradient nonlinearity. A similar relationship was observed with ADC and distance from isocenter for ROIs related to WM except the mean ADC post-correction $((0.74 \pm 0.03) \times 10^{-3} \text{ mm}^2/\text{s})$ was 6% greater than the mean reported by Helenius et al. $((0.70 \pm 0.05) \times 10^{-3} \text{ mm}^2/\text{s})$ (29) and the p-value decreased (0.0001). The p-value in this scenario however is not indicative of how well the GNLC works for WM in part because WM ADC is highly dependent on TE (37) and TE varied between patients which in turn affects ADC quantification. While CSF ADC is well established in literature, WM is less so, due to variability in tissue structure between individuals and the high dependence on diffusion parameters (37, 38). WM ADC in healthy individuals has also been reported to range anywhere between $0.6\text{--}1.05 \times 10^{-3} \text{ mm}^2/\text{s}$ (39) and so while our results were statistically different from Helenius et al., it is in general agreement with that reported in literature. The change in uniformity between ROIs and patient cases may be more appropriate to quantify the improvement in in vivo ADC due to the GNLC. The uniformity across all sampled ROIs was approximately 82% prior to correction and increased 93% after

correction for both CSF and WM. These results are encouraging as they indicate improved agreement in ADC over a range of locations within the field of view.

The variation in the locations from isocenter between patients was partially due to internal patient anatomy and the positioning of the patient within the bore and ranged from -3 to 8 cm in the inferior to superior direction. Of the 12 patient exams, 7 were considered healthy individuals with no indicated clinical findings from the radiologist's report. The other 5 volunteers had incidental findings unrelated to the quantification of the CSF and WM which is confirmed with agreement of the ADC values in literature.

While phantom and in-vivo data demonstrate promising results with GNLC, there were some limitations to our study. First, using the phantom we were able to quantify ADC at various regions in the imaging volume. However, it is not a fully complete assessment of the accuracy throughout the entire imaging volume. Second, a single imaging protocol was used and therefore, a full range of ADC values was not assessed. However, the theory of GNLC suggests that GNL effects are independent of the encoding b-value and the ADC of the measured object, and one would expect that the benefits from GNLC can be generally applied to any ADC value. This assumption does not account for a potential ADC bias introduced by noise using larger b-values. Third, we were limited to a relatively small sample size for the in vivo data set. Despite these limitations, our study quantified ADC in a number of regions in the imaging volume to provide a sufficient estimate of the accuracy in ADC estimation using GNLC. For clinical DWI, the b-value is often selected to quantify specific pathology, so we focused more on the improved uniformity before and after the GNLC.

In conclusion, the improvement in the accuracy of the ADC values demonstrated the GNL correction algorithm to be robust on the C3T scanner. The correction resulted in a more uniform ADC map for the QC phantom and a systematic shift of the mean towards the reference ground truth. In addition, GNL correction provided ADC values from the C3T scanner that were more comparable to that of the whole-body scanners. The in vivo DWI and DTI results demonstrated improved uniformity of ADC values across the same tissue type across all subjects.

Acknowledgments

The authors would like to thank Erin Gray for her assistance with gathering and processing the gradient non-linearity correction for the patient data.

Grant Support: National Institutes of Health. Grant numbers: BRP-R01-EB010065, U01-EB024450

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Figure 1.

Central axial slice of the phantom at 0°C (GE C3T):DWI image with $b=0$ s/mm² (left)

ADC map after the GNLC with PVP concentration individually labelled vials (center) and

ADC map with center, inner and outer 0% PVP vials labelled (right).

Figure 2.

Mean ADC before and after GNLC. a) Mean ADC values for the center 0% vial along the slice direction before and after GNLC correction b) Mean ADC values for the center, inner and outer 0% vials (averaged over the two central slices) c) Mean ADC values for the outer 0% vial at all 4 rotated positions (averaged over the two central slices) d) Mean ADC values for the center 0% vials at two different temperatures (averaged over the two central slices). The assumed ADC values are adopted from (25–28).

Figure 3. Phantom data from comparing C3T, MR750w and Signa HDxt 3T scanners. Mean ADC values for vials with a) 0%, b) 10%, c) 20%, and d) 30% PVP concentration were shown. The assumed ADC value is adopted from (28).

Figure 4. Patient (DWI: n=10, DTI: n=2) ADC for a) CSF before correction b) CSF after correction c) WM before correction d) WM after correction. DTI data points are identified with a black circle for each corresponding ROI.

Figure 5.

Volunteer data from C3T scanner: a) Axial mean MD maps from the two axial slices of a DTI brain scan before GNLC (left) and after GNLC (right) b) with the corresponding normalized difference ratio maps. The slice locations for the two axial slices were 2.45 cm and 7.7 cm from isocenter. The slice 7.7 cm superior to isocenter was enlarged relative to the inferior slice for better visualization, and therefore pixel size between slices are not to scale.

Figure 6. Comparison of mean ADC for a) CSF and b) WM between MR750w and C3T for one DTI patient.