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Pediatric Brain Tumor Consortium Multi-site Assessment of Apparent Diffusion Coefficient z-Axis Variation Assessed with an Ice Water Phantom

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Abstract

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Rationale and Objectives—MR diffusion imaging, can characterize physiologic characteristics of pediatric brain tumors used to assess therapy response. The purpose of this study was to assess the variability of the apparent diffusion coefficient (ADC) along z-axis, of scanners in the multicenter Pediatric Brain Tumor Consortium (PBTC).

Materials and Methods—Ice water diffusion phantoms for each PBTC site were distributed with a specific diffusion imaging protocol. The phantom was scanned four successive times to a) confirm water in the tube reached thermal equilibrium and b) allow for assessment of intra-exam ADC repeatability. ADC profiles across slice positions for each vendor and institution combination were characterized using linear regression modelling with a quadratic fit.

Results—11 sites collected data with a high degree of compliance to the diffusion protocol for each scanner. The mean ADC value at slice position zero for vendor A was 1.123×10^{-3} mm (millimeter)²/s (second), vendor B was 1.0964×10^{-3} mm²/s, and vendor C was 1.110×10^{-3} mm²/s. The percent coefficient of variation across all sites was 0.309 % (sd=0.322). The ADC values conformed well to a second order polynomial along the z-axis, (i.e., following a linear model pattern with quadratic fit) for vendor-institution combinations and across vendor-institution combinations as shown in the longitudinal model.

Conclusion—Assessment of the variability of diffusion metrics is essential for establishing the validity of using these quantitative metrics in multicenter trials. The low variability in ADC values across vendors and institutions and validates the use of ADC as a quantitative tumor marker in pediatric multicenter trials.

Keywords

diffusion phantom; MRI; pediatric brain tumors; quality assurance

1. Introduction

Pediatric brain tumors are the most common type of solid tumor among children, the second most frequent childhood malignancy after leukemia and the leading cause of death from solid tumors in this population. [1] An estimated 4452 new cases of childhood malignant brain and central nervous system (CNS) tumors are expected to be diagnosed in 2014. [2] Efforts to accrue sufficient numbers of patients for investigating more effective treatment strategies must hinge largely on multicenter trials, a defining feature of the National Institutes of Health (NIH)-funded PBTC, established in 1999. The PBTC's primary objective is to rapidly conduct novel phase I and II clinical evaluations of therapeutic drugs, new biological therapies, treatment delivery technologies and radiation treatment strategies in children from infancy to 21 years of age with primary CNS tumors. A second objective is to characterize reliable markers and predictors (direct or surrogate) of brain tumor responses to new therapies. A third objective is to develop and coordinate innovative neuroimaging techniques. Through the PBTC's Neuroimaging Center, formed in May 2000, correlative imaging endpoints and research to evaluate new therapies is in progress. [3]

MRI is the leading imaging modality for evaluating a child with a suspected brain tumor. It has unique multiplanar capabilities that offer detailed anatomical information with superior resolution and sensitivity. MRI is typically used for making a preoperative diagnosis and for

guiding treatment planning including image-guided therapies such as surgery, chemotherapy and radiotherapy. In addition, it is used for tumor follow-up, for evaluating disease progression, and for assessing both treatment response and effects of therapy.

Lacking with conventional MR is an assessment of physiological and functional information about the tumor. Advanced MR imaging techniques, including MR diffusion imaging, can elucidate and characterize the physiologic characteristics of pediatric brain tumors and can be used to assess response to therapy. MR diffusion using predominantly echo-planar techniques has been useful in the characterization of tissue, tumor cellularity, tumor grading, tumor response to treatment, and distinction of tissue types. [4-6] It has also been used as a biomarker for detecting early treatment response in brain tumor patients and thus is often incorporated into the imaging evaluation of these patients. [7]

In addition to standardization of imaging acquisition protocols in the multicenter setting, assessment of the variability of imaging metrics due to technical limitations is essential for establishing the precision of quantitative measurements of these metrics in multicenter trials. Our initial work focused on the assessment of imaging metrics using standard MR sequences and the American College of Radiology (ACR) phantom. [8] Other groups have realized the importance of quality assurance in cohort studies, as currently performed in Europe.[9] As diffusion imaging is an integral component of the majority of the PBTC multicenter trials, we sought to validate MR diffusion data from the 11 participating sites by using an ice water phantom created for this purpose[10,11] and tested for the first time in a multicenter consortium.

2. Materials and Methods

2.1 Data Collection

Eleven sites with a total of 15 scanners from three major vendors (vendors A, B and C not necessarily in alphabetical order) participated in the study. An ice water diffusion phantom (Figure 1) consisting of a sealed 29 mm diameter tube of distilled water within a larger plastic jug to contain ice cubes and tap water was distributed to each site along with instructions for its use as a diffusion phantom and recommendations for a specific diffusion imaging protocol. Also included were instructions for preparing the ice water diffusion phantom and allowing sufficient time for cooling of the central tube to approximately 0° Celsius (C) along its full length. The advantage of an ice water-based diffusion phantom is to maintain the water at a known temperature, thereby establishing an absolute and well-known diffusion coefficient (e.g. $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$ for water at 0°C) along the length of the central tube. [10] The recommended protocol included use of single shot echo-planar imaging diffusion sequences employing three orthogonal diffusion sensitization directions with one baseline and one high (1000 s/mm^2) b-factor for the generation of trace ADC images in the axial plane along the full length of the ice water diffusion phantom. The recommended protocol and range of sequence parameters are listed in the top row of Table 1. Sites were instructed to scan the cooled phantom four times in succession to a) confirm water in the measurement tube had reached thermal equilibrium with ADC values not showing a downward trend and b) to allow for assessment of intra-exam ADC repeatability.

Sites were requested to send vendor-generated ADC maps to the PBTC Neuroimaging Center for analysis.

2.2 Data Analysis

A Region of Interest (ROI) analysis was used to determine the ADC value for each slice along the central tube. The range of ROI areas employed was 53.1 to 62.2 mm², and the average ROI area was 59.4 mm². Due to differences in phantom positioning across sites, the true zero, or isocenter, along each scanner's z-axis was determined from the localizer images and the central slice of the tube was repositioned to this origin for consistency of mean ADC values along the z-axis for all sites.

2.3 Statistical Considerations

Diffusion phantom ADC profiles along the z-axis across the slice positions for each vendor and institution combination were characterized using linear regression modelling with a quadratic fit. To describe the overall diffusion phantom ADC profile over the slice positions across vendors and institutions, a random coefficients model was constructed assuming random slope and intercept for each vendor-institution combination and assuming autoregressive-1 variance-covariance structure, utilizing all available data. Model adequacy was checked through residual diagnostics both in the individual linear regression models and in the random coefficients model. For each scanner and at each slice position along the z-axis, the four separate measurements of ADC were averaged to obtain a mean and sd from which the coefficient of variation at each slice position was calculated as a percentage using $100 \times \text{sd}/\text{mean}$, providing a measure of ADC reproducibility at each location.

3. Results

Diffusion phantom data were obtained from 15 institution-vendor combinations where six institutions used vendor A (denoted A1-A6), five institutions used vendor B (denoted B1-B5) and four institutions used vendor C (denoted C1-C4). To magnify the model estimates in quadratic linear regression models, we multiplied the diffusion phantom ADC values by 100. Representative plots of ADC vs slice position are shown in Figure 2.

Of the 15 scanners, 13 were 3 Tesla (T) scanners and 2 from vendor A were 1.5 T scanners. All 11 sites collected data using the ice water diffusion phantom with a high degree of compliance to the requested diffusion imaging protocol, as shown for each site and scanner in Table 1. At one site the phantom was only scanned once as opposed to all 4 times (this data was included and is represented in Table 2, vendor-institution B3 because there was minimal variation between the 4 scanning sessions, which is reflected by very comparable intercept, linear and quadratic effect estimates for B3 like others as well as the model R²). All scanners provided data for the 27 axial slices, resulting in 108 ADC data points per scanner with the exception of 27 ADC data points from one scanner. A total of 1,539 ADC values were thus collected. An example of the normalization of ADC values along the z-axis is shown for one site. (Figure 3) The individual model fit for each scanner is provided in Table 2. The longitudinal model fit for each vendor is provided in Table 3. The mean ADC value at slice position zero (z=0) for vendor A was 1.123×10^{-3} mm²/s, vendor B was 1.0964

$\times 10^{-3} \text{ mm}^2/\text{s}$, and vendor C was $1.110 \times 10^{-3} \text{ mm}^2/\text{s}$. The coefficient of variation, defined as $[(\text{sd}/\text{mean}) \times 100]$, across all sites was 0.309 % (sd=0.322).

The ADC values were found to conform well to the second order polynomial (i.e., following a linear model pattern with quadratic fit) for most vendor-institution combinations (Table 2) as well as across vendor-institution combinations as shown in the longitudinal model. (Table 3) Both linear and quadratic effect of slice position were significant and the models adequately characterized the slice position variation in diffusion phantom ADC measurements. This model also suggested that vendor A had significantly higher ADC values compared to vendor C (mean $\pm$ standard error= 1.00 ± 0.263), and that vendor B had significantly lower ADC values on average (mean $\pm$ se= -1.85 ± 0.28) compared to vendor C (Table 3, Figure 4), though the differences are small.

The %coefficient of variation of ADC values were more stable across slice positions for vendor A and C compared to B as shown in Figure 5. The sd of coefficient of variation ranged from 0.03 to 0.17 % for vendor A, from 0.07 to 0.58 % for vendor B, and 0.04 to 0.10 % for vendor C. Overall, vendor A and C had relatively lower coefficient of variation values on average, ranging from 0.08 to 0.52 % (vendor A), 0.08 to 0.25 % (vendor C) compared to vendor B with mean coefficient of variation ranging from 0.14 to 0.93 % (Figure-5).

4. Discussion

A primary goal of the PBTC is to gauge response to therapy using quantitative neuroimaging methods. MRI is well-suited to this task and a number of quantitative parameters are available for tissue characterization, including the relaxation times T1, T2 and T2* as well as diffusion-associated parameters, the most prominent being the trace ADC as acquired with single-shot echo-planar imaging sequences now common to most scanners. Understanding and accounting for instrumental sources of error in ADC measurement is critical in determining whether observed changes in tumor ADC values are due to a biological response or reflect measurement error. Such considerations motivated this work in which ADC values from multiple scanners participating in PBTC clinical trials were measured systematically along the central, long axis z-dimension of an ice water phantom specifically designed for this purpose. When sufficiently chilled to temperatures just above 0° C, the ADC values along the length of the central tube of distilled water is known to be $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$. Our overall results record ADC values within ~ 10 % of this value for 97.6% of the measurements for vendor A, 98.5% for vendor B, and 93.5% for vendor C. At slice position-0, all three vendors had measurements within less than 5% of $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$ (Figure 2). These results provide an approximate bound from which to gauge longitudinal biological responses as real or potentially due to systematic error. If a tumor is sequentially scanned in precisely the same location of a particular scanner, then a better measure of the systematic error is given by the reproducibility results from the 4 scans at each location from all sites. With mean ADC % coefficient of variation values this would make for even lower bounds on the order of 1%, though for in vivo brain studies, physiological noise including voluntary and involuntary (e.g. cerebrospinal fluid pulsations) may be anticipated to increase the margin of error beyond that gleaned from our

reproducibility data. It is also clear from the data that the general drift of ADC with z from isocenter is well-characterized with 2nd order polynomial functions. The main source of observed z-dependent ADC is believed to be gradient nonlinearity wherein the local gradient strength varies spatially, thereby creating a spatially-dependent bias in measurements. [10-12] If characterized for any given scanner, the coefficients of the quadratic polynomial could be used to make small z-dependent corrections to tumor ADC values, eliminating changes in tumor location along z as a source of error in longitudinal studies designed to gauge treatment response.

The current study has several limitations worth mentioning. One limitation is, of course, the relatively small set of scanners - 15 - further divided among three vendors, though differences between vendors or their characteristic ADC vs z plots do not appear very dramatic. Furthermore, we did not assess spatial variations in ADC for the different diffusion sensitization gradient directions but rather focused on the trace ADC values as they are the primary clinical indices of interest. More involved studies of the variations for the individual diffusion sensitization directions could be performed in efforts to characterize and correct for errant b-factors and may prove useful when considering advanced diffusion imaging methods such as diffusion tensor imaging and the related diffusion tractography [13]. Another limitation is the restriction of the current measurements to the central z-axis of the x-y plane in scanner coordinates. Future studies now begun with a specialized ice water phantom cradle are allowing for height adjustments of the central tube within the bore, and so will provide for further spatial assessments of ADC variations and subsequent improved correction schemes. [14]

4.1 Conclusion

To conclude, it is rather remarkable that variations of ADC along the z-axis for approximately 200 mm along the z-axis show such small variations (Figure 2) and that ADC measures at each location are highly reproducible (Figure 5). Furthermore, the z-variations may be accounted for with a relatively simple polynomial equation from which corrections for this effect may be made. In addition, this study shows low variability in ADC values across vendors and institutions and validates the use of ADC as a quantitative tumor marker in both pediatric and adult multicenter trials. The characterization of such spatial variations of ADC values may also help motivate the major vendors towards efforts to improve b-factor assessments throughout the scanner bore and so eliminate this type of error at the source. Our results, which generally show systematically lower ADC values at the further ends of the z-axis, suggest that careful positioning of the head along the central portions of the z-axis will yield the most accurate ADC values, a feature of particular interest in the pediatric setting where small head sizes/circumferences can readily accommodate such optimal positioning.

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References

1. Gurney, J.; Smith, M.; Bunin, G. CNS and miscellaneous intracranial and intraspinal neoplasms. In: Ries, L.; Smith, M.; Gurney, J., editors. Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995 NIH Publication No 99-4649. Bethesda, MD: National Cancer Institute SEER Program; 1999. p. 51-63.
2. Central Brain Tumor Registry of the United States in 2006-2010 (CBTRUS). Nov 2013 Primary brain and central nervous system tumors diagnosed in the United States. Hinsdale, IL: National Program of Cancer Registries; 2014.
3. Poussaint TY, Phillips PC, Vajapeyam S, et al. The Neuroimaging Center of the Pediatric Brain Tumor Consortium-collaborative neuroimaging in pediatric brain tumor research: a work in progress. *AJNR Am J Neuroradiol*. 2007; 28:603–7. [PubMed: 17416804]
4. Chenevert TL, Meyer CR, Moffat BA, et al. Diffusion MRI: a new strategy for assessment of cancer therapeutic efficacy. *Mol Imaging*. 2002; 1:336–43. [PubMed: 12926229]
5. Chenevert TL, Ross BD. Diffusion imaging for therapy response assessment of brain tumor. *Neuroimaging Clin N Am*. 2009; 19:559–71. [PubMed: 19959005]
6. Gauvain KM, McKinsty RC, Mukherjee P, et al. Evaluating pediatric brain tumor cellularity with diffusion-tensor imaging. *AJR Am J Roentgenol*. 2001; 177:449–54. [PubMed: 11461881]
7. Padhani AR, Liu G, Koh DM, et al. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. *Neoplasia*. 2009; 11:102–25. [PubMed: 19186405]
8. Mulkern RV, Forbes P, Dewey K, et al. Establishment and results of a magnetic resonance quality assurance program for the pediatric brain tumor consortium. *Acad Radiol*. 2008; 15:1099–110. [PubMed: 18692750]
9. Workshop on Population Imaging, March 25, 2010. The Hague; The Netherlands: Available at <http://www.populationimaging.eu> [Accessed October 5, 2014]
10. Chenevert TL, Galban CJ, Ivancevic MK, et al. Diffusion coefficient measurement using a temperature-controlled fluid for quality control in multicenter studies. *J Magn Reson Imaging*. 2011; 34:983–7. [PubMed: 21928310]
11. Malyarenko D, Galban CJ, Londy FJ, et al. Multi-system repeatability and reproducibility of apparent diffusion coefficient measurement using an ice-water phantom. *J Magn Reson Imaging*. 2013; 37:1238–46. [PubMed: 23023785]
12. Malyarenko DI, Ross BD, Chenevert TL. Analysis and correction of gradient nonlinearity bias in apparent diffusion coefficient measurements. *Magn Reson Med*. 2014; 71:1312–23.
13. Mulkern RV, Davis PE, Haker SJ, et al. Complementary aspects of diffusion imaging and fMRI; I: structure and function. *Magn Reson Imaging*. 2006; 24:463–74. [PubMed: 16677953]
14. Malyarenko D, Newitt D, Tudorica A, et al. Quantitative Imaging Network Demonstration of ADC Nonlinearity Bias in Multi-center Trials. *Proc Intl Soc Mag Reson Med*. 2014; 22:4506.

Figure 1.

Representative sagittal T1 (left) and axial ADC (right) images of the diffusion ice water phantom. Red line in the sagittal image shows the central slice along the tube to which ADC values were referenced, regardless of the actual slice positioning proscribed. In the ADC image a typical ROI within the distilled water tube used for data analysis is shown. ADC, apparent diffusion coefficient; ROI, Region of Interest;

Figure 2.

Representative Plots of ADC vs slice position (SP) [x-axis = slice position in mm; y-axis = $\text{ADC} \times 10^{-5} \text{ mm}^2/\text{s}$] from each vendor (left-to-right) with one strong (top) and one weak (bottom) quadratic profile, respectively, along the tube.

ADC, apparent diffusion coefficient; mm, millimeter, s, second; SP, slice position

Figure 3.

Plot of ADC vs slice position (SP) along the tube for one site before (red squares) and after (blue diamonds) normalization along the z-axis using the localizers for fixing the isocenter.

[x-axis = slice position in mm; y-axis = $\text{ADC} \times 10^{-5} \text{ mm}^2/\text{s}$]; the model fit is

$$\text{ADC} = 112.7 + 0.0186 \cdot \text{SP} - 0.0019 \cdot \text{SP}^2.$$

ADC, apparent diffusion coefficient; mm, millimeter; s, second; SP, slice position

Figure 4.

Fit plot for Diffusion phantom ADC values across vendors; [x-axis = slice position in mm; y-axis = $\text{ADC} \times 10^{-5} \text{ mm}^2/\text{s}$].

ADC, apparent diffusion coefficient; mm, millimeter; s, second

Figure 5.
Percent Coefficient of Variation Profile by Site-vendor combinations.

Table 1
MR Recommended Imaging Parameters for Diffusion Phantom (top row) with Site Compliance Figures (subsequent rows)

Site	Vendor	Field Strength T	Field of View (mm)	Acquisition Matrix	Reconstruction Matrix	Orientation	Quantity of slices	TR (ms)	TE (ms)	Number Gradient directions	Frequency encoding bandwidth per pixel (Hz)
Requested Protocol	A, B, C	3.0	240 × 240	128 × 128	256 × 256	axial	27	6000	75-100	3 orthogonal axes	1500-2500
A1	A	3.0	240 × 240	128 × 128	256 × 256	axial	27	6000	72.5	3	1953.12
A2	A	1.5	239 × 239	128 × 128	256 × 256	axial	27	6000	66.7	3	1953.12
A3	A	1.5	279 × 279	128 × 128	256 × 256	axial	27	8000	80.8	3	1953.12
A4	A	3.0	239 × 239	128 × 128	256 × 256	axial	27	6000	67.3	3	1953.12
A5	A	3.0	239 × 239	128 × 128	256 × 256	axial	27	8000	87.3	3	1953.12
A6	A	3.0	239 × 239	128 × 128	256 × 256	axial	27	6000	67.3	3	1953.12
B1	B	3.0	238 × 238	128 × 128	256 × 256	axial	27	6000	89.2	3	2288
B2	B	3.0	240 × 240	128 × 128	256 × 256	axial	27	6000	100	3	2410
B3	B	3.0	239 × 239	128 × 128	256 × 256	axial	27	6000	75	15	2408
B4	B	3.0	239 × 239	128 × 128	256 × 256	axial	27	7000	89.6	3	2349
B5	B	3.0	239 × 239	128 × 128	256 × 256	axial	27	7000	89.6	3	2410
C1	C	3.0	240 × 240	130 × 130	260 × 260	axial	27	6000	84	3	1830
C2	C	3.0	239 × 239	130 × 130	260 × 260	axial	27	7000	92	3	1605
C3	C	3.0	239 × 239	130 × 130	260 × 260	axial	27	6000	93	3	1672
C4	C	3.0	240 × 240	128 × 128	128 × 128	axial	27	9400	101	3	1345

A1 – A6, vendor A; B1 – B5, vendor B; C1 – C4, vendor C; Hz, Hertz; MR, Magnetic Resonance; T, Tesla; TE, echo time; TR, relaxation time

Table 2
Individual model quadratic regression fits for ADC values for each vendor-site combination

Vendor-Institution	Intercept (p-value)	Linear Effect (p-value)	Quadratic Effect (p-value)	R ²
A1	112.23 (<0.0001)	0.0180 (0.0042)	-0.0025 (<0.0001)	0.950
A2	111.10 (<0.0001)	-0.0301 (<0.0001)	-0.0008 (<0.0001)	0.863
A3	113.08 (<0.0001)	-0.0084 (0.0011)	-0.0014 (<0.0001)	0.969
A4 A5	112.43 (<0.0001) 112.70 (<0.0001)	0.0343 (<0.0001) 0.0186 (<0.0001)	-0.0005 (<0.0001) -0.0019 (<0.0001)	0.773 0.994
A6	114.21 (<0.0001)	0.0055 (0.17)	-0.0005 (<0.0001)	0.718
B1	111.32 (<0.0001)	0.0157 (0.0011)	-0.0012 (<0.0001)	0.961
B2	107.65 (<0.0001)	0.0147 (0.0295)	-0.0008 (<0.0001)	0.772
B3	109.83 (<0.0001)	0.0164 (<0.0001)	-0.0009 (<0.0001)	0.974
B4	109.08 (<0.0001)	0.0204 (<0.0001)	-0.0017 (<0.0001)	0.968
B5	110.29 (<0.0001)	0.0107 (0.0037)	-0.0011 (<0.0001)	0.927
C1	111.56 (<0.0001)	-0.035 (<0.0001)	-0.0013 (<0.0001)	0.945
C2	111.19 (<0.0001)	-0.0144 (0.0075)	-0.0018 (<0.0001)	0.997
C3	109.44 (<0.0001)	0.0035 (0.0707)	-0.0004 (<0.0001)	0.759
C4	112.51 (<0.0001)	-0.0134 (<0.0001)	-0.0013 (<0.0001)	0.950

A1 – A6, vendor A; ADC, apparent diffusion coefficient; B1 – B5, vendor B; C1 – C4, vendor C; R², r squared

Table 3

Random Coefficients Model for ADC values across sites.

Effect	Estimate	Standard Error	P-value
Intercept (SP=0) for vendor C (Reference Group)	111.44	0.23	<.0001
Intercept Difference for vendor A compared to C	1.00	0.263	0.0002
Intercept Difference for vendor B compared to C	-1.85	0.28	<.0001
Slice Position	0.0083	0.0069	0.2549
Slice Position ²	-0.00116	0.000048	<.0001

ADC, apparent diffusion coefficient; SP, Slice Position