Icewater for Quality Control of Diffusion Measurements in Multi-Center Trials

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Introduction

Apparent diffusion coefficient (ADC) is sensitive to therapy-induced change in tumor cellularity, therefore ADC has been proposed as a treatment-response biomarker. Prerequisites for use of ADC, as well as any image-based biomarker in multi-center trials is standardization of data acquisition/analysis, and certification of sites/systems via quantitative measurements on known test objects [1]. A variety of diffusion phantoms have been proposed [2-5], although consensus in design and materials has not been achieved to date. Regardless of the choice of diffusing media, control and/or determination of temperature is required since diffusion is a function of temperature. The objective of this study is to assess reproducibility of ADC measurements performed at multiple sites on various clinical platforms using a simple universal temperature-controlled fluid - icewater.

Material and Methods

A 175x175x200mm test object was designed to hold five 28mm diameter tubes filled with distilled water suspended within icewater. Once thermal equilibrium is reached, the icewater maintains the measurement volume in the tubes at 0 ^{o}C for an extended period thus provides a fluid at a known diffusion coefficient ($1.1x10^{-3}mm^2/s$). A tube filled with a sucrose solution was also included to provide ADC contrast. Twenty test objects were constructed and distributed to institutions in North America and Europe with explicit ice-filling and scan instructions. The scan protocol was designed for compatibility across most modern clinical MRI systems: DW SS-EPI; TR/TE=8000/100+/-10ms; 128x128 acq matrix; 240mm FOV; 25, 6mm slices; at b=0,500,800,1000,2000s/mm^2. Head coil and torso scans were performed including scans with the test object offset ±110mm in R/L direction to further assess spatial dependencies. MatLab scripts were developed to import Dicom DWI regardless vendor brand and image sort order for conversion to a uniform structure format for reduction to ADC maps and ROI analysis.

Results

Data were returned from 34 MRI systems, although 5 were dropped due to significant protocol discrepancies leaving usable datasets from: Vendor A (1.5T N=3; 3T N=3); Vendor B (1.5T N=6; 3T N=10); Vendor C (1.5T N=3; 3T N=4). Results of mean diffusion coefficient from circular ROIs of the central tube on central slices are illustrated in Figure 1. Boxplots are separated by vendor and b-value pairs, although 1.5T and 3T data were combined for simplicity. Horizontal dashed lines represent ±5% from the assumed correct diffusion value of $1.1x10^{-3}$ mm^2/s, and illustrate that 27 of the 29 systems produced diffusion values within 5% of the correct value. One system (a Vendor A 3T) was a clear outlier (~70% error) for 3 of 4 b-value pairs. Excluding this outlier, the standard deviation over all measurements (vendor, b-value pair, and field strength) was below 3% of the correct value. However there frequently was a significant systematic spatial dependence of measured diffusion as exemplified by one system in Figure 2 for right-left offsets and superior-inferior offsets (Figure 3). As before, the horizontal lines represent the assumed correct value and ±5% from this value.

Figure 1

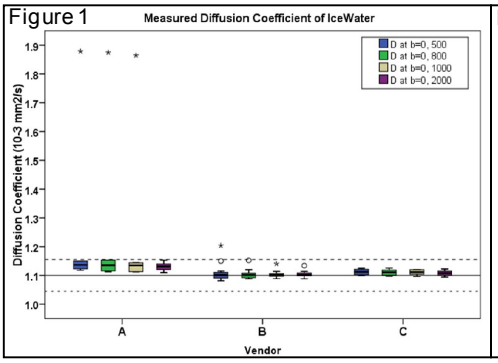


Figure 2

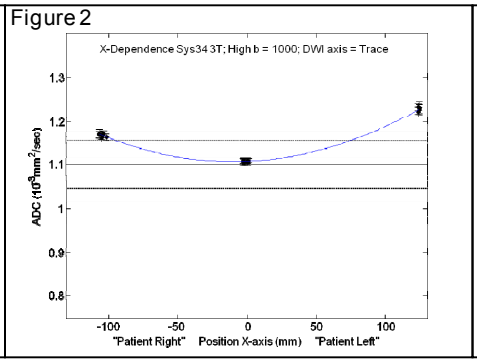
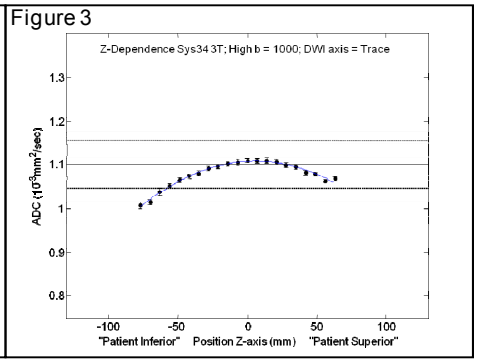


Figure 3



Conclusion

Qualification of systems to perform ADC measurements will be an essential element for QC in clinical trials using ADC as a biomarker. For lack of an establish diffusion phantom standard, this study utilized icewater for initial assessment of ADC reproducibility across clinical MR platforms. Identification of system outlier(s) and 3-5% reproducibility in diffusion coefficient measurement exclusive of outliers was demonstrated. Systematic spatial-dependent error was also demonstrated with its source under investigation.

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