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# Assessing diffusion kurtosis tensor estimation methods using a digital brain phantom derived from human connectome project data



Daniel V. Olson<sup>a,\*</sup>, Volkan E. Arpinar<sup>b</sup>, L. Tugan Muftuler<sup>c</sup>

<sup>a</sup> Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, USA

<sup>b</sup> Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, USA

<sup>c</sup> Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, WI, USA

## ARTICLE INFO

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### ABSTRACT

*Purpose:* Diffusion kurtosis imaging (DKI) has gained popularity in recent years as an advanced diffusion-weighted MRI technique. This work aims to quantitatively compare the performance and accuracy of four DKI processing algorithms. For this purpose, a digital DKI brain phantom is developed.

*Methods:* Data from the Human Connectome Project database were used to generate a DKI digital phantom. In a Monte Carlo Rician noise simulation, four DKI processing algorithms were compared based on their mean squared error, squared bias, and variance.

*Results*: Algorithm performance was region-dependent and differed for each diffusion metric and noise level. Crossover between variance and squared bias error occurred between signal-to-noise ratios of 30 and 40.

*Conclusion:* Through the framework presented here, DKI algorithms can be quantitatively compared via a ground truth data set. Error maps are critical as algorithm performance varies spatially. Bias-plus-variance decomposition provides a more complete picture than MSE alone. In combination with refinements in acquisition in future studies, the accuracy and efficiency of DKI will continue to improve promoting clinical adoption.

#### 1. Introduction

Diffusion kurtosis imaging (DKI) is becoming increasingly popular among MRI diffusion-weighted imaging methods due to its higher sensitivity to tissue microstructure compared with conventional diffusion tensor imaging, while remaining within a clinically feasible scan time [1,2]. However, the kurtosis tensor model is sensitive to noise and other data artifacts [3–5]. Slight irregularities in the signals can translate to large errors in the model-derived metrics. Signal dropout and black voxels are common [6]. If DKI is to be employed as a reliable and reproducible biomarker, mitigating these artifacts is critical.

To address problems arising from noise, various algorithms and processes have been introduced that attempt to minimize the effects of erroneous signals. These algorithms target different stages of the DKI processing pipeline and include preconditioning the signal [7,8], removing outlier signals based on residuals [6], and applying adaptive or fixed constraints to the fitting algorithm [9–11]. With such a diversity in approaches, it is challenging to determine the optimal approach without a ground truth data set. To test and validate DKI methods, various groups have used phantoms [12–15], in vivo data [16–19], and

simulations [20–23]. However, a more realistic and comprehensive digital DKI phantom based on in vivo brain data is desired for a fair and generalizable comparison of algorithm performances. For this purpose, more advanced diffusion simulations and phantoms that have been developed for the assessment of DTI and tractography could be adapted to DKI [24–27].

The study presented here aims to evaluate various DKI reconstruction methods using a simple, yet robust, digital phantom. To achieve this goal, we first generated a synthetic digital diffusion MRI data set that incorporated q-space data from 10 subjects from the Human Connectome Project (HCP) database [28]. Then, we compared the performances of four DKI algorithms on a voxelwise basis via mean square error (MSE) and bias-plus-variance decomposition to determine the optimal algorithm for parameter estimation from a typical DKI data set.

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Abbreviations: MK, mean kurtosis; Kax, axial kurtosis; Krad, radial kurtosis; SVD, singular value decomposition; DKE, diffusional kurtosis estimator; DWAR, directional weighting and regularization; WM, white matter

<sup>\*</sup> Corresponding author at: Department of Biophysics, Medical College of Wisconsin, 8701 West Watertown Plank Road, Milwaukee, WI 53226, USA. *E-mail address:* olsondv@gmail.com (D.V. Olson).

Fig. 1. Overview of the DKI phantom generation.



## Table 1

Means and standard deviations (in parentheses) for the digital DWI brain phantom and the group.

	MD (*10 <sup>-3</sup> s/ mm <sup>2</sup> )	FA	МК	Kax	Krad
Phantom	0.85 (0.06)	0.47	1.11	0.83	1.47
		(0.12)	(0.12)	(0.10)	(0.30)
Group	0.84 (0.08)	0.47	1.06	0.80	1.40
		(0.12)	(0.13)	(0.11)	(0.31)

# 2. Methods

# 2.1. Ground truth diffusion MRI data set

Preprocessed T1-weighted and diffusion-weighted images (DWI) of 10 healthy subjects (six females/four males, 22–30 years old) from the Washington University in Saint Louis–University of Minnesota HCP database [28] were used to generate the digital phantom data set used in this work. An overview of the workflow is illustrated in Fig. 1.

The HCP DWI protocol is based on spin-echo echo-planar imaging with the following parameters: TR/TE: 5520/89.5 ms; flip angle: 78 deg.; refocusing flip angle: 160 deg.; FOV:  $210 \times 180$ ; matrix:



**Fig. 2.** Phantom DKI metric images (top). Normalized histograms of metrics in white matter voxels with an FA > 0.3. Phantom (black), the group (blue), and a single subject (red). Units for mean diffusivity are (mm/s<sup>2</sup>). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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