An Anisotropic Diffusion Phantom for Improved Applications in Diffusion-Weighted Imaging and Potential Applications as Part of a Quality Control System
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Advances in medicine have supported and increased the range of possible interventions available to clinicians, enabling them to provide the best possible healthcare to their patients. Despite this, limitations and inefficiencies of the systems used impose barriers on improvement in quality of care.

In the medical imaging space specifically, there is a growing need for quality control tracking in the form of real-time scan quality reports and longitudinal scanner performance analysis. This need is based in both economics and patient care: efficient and high quality data and tools are paramount to the delivery of high quality, effective and affordable healthcare. In neurosurgery, having confidence in imaging data is imperative to the clinical decision making process. Specifically, the application and importance of diffusion weighted imaging (DWI) is steadily growing as an important tool supporting improved patient outcomes [1]. DWI measures the 3D diffusion pattern of water molecule displacement through the porous network of cerebral structures to infer connectivity, axon fiber architecture, and tissue integrity [2]. It is utilized for non-invasive diagnosis of neurological tissue abnormalities, trauma assessment, tumor resection planning, and functional connectivity assessment, providing diagnostic utility for tissue conditions where the diffusion of water is disrupted [3].

Despite the promise of DWI, its practicality can be compromised by various factors, including high sensitivity to motion and magnetic field strength inhomogeneities, which can lead to image quality degradation, inaccurate geometric representation, and inability to successfully co-register to anatomical imaging. Additionally, during post processing, diffusion protocols can reverse right-left orientation of tractography before co-registration with primary series. The implications of these factors are significant as they can contribute to loss of diagnostic sensitivity, and can negatively impact patient care if these inaccurate data are used for surgical planning and clinical decision making.

A means of demonstrating correct hardware and software function is essential as most adverse effects, with the exception of physiological noise, are directly related to scanner performance and may be time-variant and scanner-dependent [4]. There is a need to validate and verify the results obtained from DWI techniques before they are used to aid in clinical decision making or surgical intervention, however, there is no consensus for an appropriate assessment. Although various ad hoc phantoms...
have been developed in academia, there is no commercially available standard that can be used with DWI protocols [5-9]. A phantom, bio-mimicking a temporally stable neuro-architecture, would allow for standardized and rigorous assessment across systems and image processing software and improve reproducibility and temporal stability. In both a clinical and research setting, radiologists, neurologists and neurosurgeons could use an anisotropic diffusion phantom to establish and monitor the baseline performance of MRI systems and enable the quantification of their performance for multi-site and longitudinal studies. The precision, or within-scan variability, can be estimated via statistical means [4]. Additionally, an anisotropic diffusion phantom may enable testing, validation, and optimization of current and work-in-progress DWI pulse sequences [10, 11], aid in the development of standardized DWI-specific QA/QC routines to calibrate MR systems [12, 13], improve the effectiveness of data integration in multi-site scanning trials [14, 15], and enable testing, validation, and optimization of tractography algorithms [5, 8, 16].

This white paper describes a novel anisotropic diffusion phantom intended to support improved diffusion imaging.

**ANISOTROPIC DIFFUSION PHANTOM**

*Synaptive Medical* has developed a biomimetic phantom containing complex geometries that mimic the tissues of the body where anisotropic diffusion of water exists. The aim of the *Synaptive Medical Anisotropic Diffusion Phantom* (Figure 1) is to support the utility and application of DWI as a diagnostic decision-making tool for researchers and clinicians.

The phantom consists of flexible bundles aligned in orthogonal planes as well as curved and kissing pathways to mimic the orientation of the fascicles of nerve fibers in the brain. Each fiber bundle contains a highly ordered substructure that is quantifiable and scalable. The dimensions of the fiber bundle substructure is on a magnitude comparable to the substructure of nervous tissue allowing patient safe protocols to be benchmarked [17]. The product is scaled to fit
within all commercial head coils and includes orientation reference lines for correct scanner placement and localization.

RESULTS

MR scans were performed on the phantom on both Philips (1.5T) and Siemens (3T) scanners. An example of a patient safe, clinical diffusion-weighted sequence is described. The phantom was imaged using a 2D EPI DTI sequence: 3T Siemens Skyra; 32 channel head coil; TE/TR = 119.0/20300 msec; Matrix = 128x128; FOV = 16.6 cm (1.3 x 1.3 mm in-plane resolution), 126 slices; slice thickness = 1.3 mm (no gap); grappa = 2; partial Fourier off; 20 diffusion directions; b = 1000 mm²/sec, and a 2D T2-weighted sequence: TE/TR = 180.0/15900 msec; Matrix = 192 x 192; FOV: 16.5 cm (0.86 x 0.86 mm in-plane resolution), 126 slices; slice thickness = 1.0 mm (0.3 mm gap). Data processing was performed using BrightMatter™ Plan, a surgical planning tool that automatically co-registers DWI data to a T1-weighted, T2-weighted, or CT image and generates whole brain 3D tractography [1, 18].

In the current work the diffusion-weighted images were co-registered with the acquired T2-weighted images. Figure 2a and 2b display coronal slices of the T2-weighted images for the interweaving fiber bundles with and without the overlaid tractography. The tractography generated occupies the entire fiber bundle dimensions. Complete phantom tractography is shown in Figure 2c.

Figure 2: Synaptive BrightMatter™ Plan images using the Synaptive Anisotropic Diffusion Phantom: (a) coronal slice of T2-weighted images, (b) overlay of generated tractography on to T2-weighted images, (c) generated tractography for the entire phantom.
Tractography statistics were also extracted to obtain mean fractional anisotropy (FA) of the tracts for individual fiber bundles. Figure 3 displays the average FA values for slices along the x-direction fiber bundles (top two red coloured fibers in Figure 2c). These fiber bundles have a mean FA of 0.41 and 0.38 with standard deviations of 0.09 and 0.08, respectively. The physical volume of the fiber bundles is 2400 mm$^3$ and the volume of voxels occupied by the tractography are 2300 and 2200 mm$^3$, respectively, confirming the tractography covers the entire fiber bundle volume. In addition, Figure 3 demonstrates the consistent FA values throughout the entire length of the fiber bundles.

We have demonstrated a novel anisotropic diffusion phantom, capable of generating the anisotropic diffusion of water comparable to white matter fascicles, using highly organized and flexible fiber bundles. The application of this phantom may, as part of a quality assessment tool, contribute to improved diagnostic and pre-surgical imaging, clinical outcomes and economic efficiencies in healthcare.

Furthermore, it aligns with the goal of expanding the application of diffusion-weighted imaging protocols to other indications. Potential applications include: differentiation of glioma and metastatic tumour margins from cerebral parenchyma based on analysis of peritumoral DTI, stroke severity and multiple sclerosis diagnoses from decreasing FA metrics and differential diagnosis of spinal
astrocytoma and ependymoma based on their infiltration or displacement of fibers [19].

With the rise in large, multi-site and longitudinal research studies, and the increased use of diffusion-weighted imaging in a clinical setting, the importance of verifiable quality assessment tools for MR imaging has never been more important.


