

## Introducing QuantConn

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# Introducing QuantConn: Overcoming Challenging Diffusion Acquisitions with Harmonization

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**Abstract.** White matter alterations are increasingly implicated in neurological diseases and their progression. Diffusion-weighted magnetic resonance imaging (DW-MRI) has been included in many international-scale studies to identify alterations in white matter microstructure and connectivity. Yet, quantitative investigation of DW-MRI data is hindered by a lack of consistency due to variations in acquisition protocols, sites, and scanners. Specifically, there is a need to harmonize the preprocessing of DW-MRI datasets to ensure that compatible and reproducible quantitative metrics are derived from each site, including (1) bundle-wise microstructure measures, (2) features of white matter fiber bundles, and (3) connectomics measures. In the MICCAI CDMRI 2023 QuantConn challenge, participants are provided raw data from the same individuals taken with two different acquisition protocols on a single 4 tesla scanner in the same scanning session and asked to preprocess the data in order to minimize acquisition differences while retaining biological variation. Here, we outline the testing framework, provide baseline pre-harmonized results, and discuss the learning implications of this challenge.

**Keywords:** Diffusion MRI · harmonization · macrostructure · microstructure · tractography · connectome · image processing

## 1 Introduction

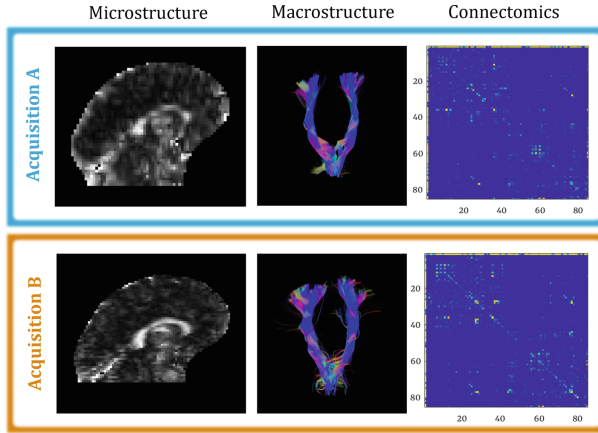
Diffusion-weighted magnetic resonance imaging (DW-MRI) is a non-invasive imaging modality that enables in-vivo modeling of white matter microstructure and facilitates structural brain connectivity mapping. DW-MRI has been included in many international-scale studies focused on white matter biomarkers in development, disease, and disorders. Yet, multi-site investigation of DW-MRI data is hindered by a lack of consistency due to variations in acquisition protocols, scanner settings, and manufacturers [17]. Substantial progress has been made with calibration and harmonization to reduce inter-subject variance and improve the interpretability of computed measures. However, the fundamental challenge remains that the clinical application of DW-MRI (as currently implemented) is confounded by inter-scanner and inter-site effects. Here, we introduce the QuantConn challenge - an international community challenge which aims to harmonize differences in diffusion acquisitions.

This challenge builds off the successful SuperMUDI [15] and MUSHAC [13] challenges. In SuperMUDI, participants were tasked with super-resolving data ( $N=5$  volunteers) that have high in-plane resolution but thick (axial) slices in order to match an isotropically acquired dataset. In the MUSHAC challenge, participants were given datasets ( $N=15$  volunteers) that were acquired on two different scanners, with two different acquisitions on each, and tasked with minimizing cross-scanner and cross-protocol differences in voxel-wise indices. Here, we provide 103 pairs of datasets of the same subjects, scanned with very different acquisition protocols - and challenge participants to minimize differences in the data in order to minimize differences in microstructure, tractography bundle analysis, and connectomics measures. The key innovations of the QuantConn challenge are (1) we assess bundles and tractography in the context of harmonization for the first time, (2) we assess connectomics in the context of harmonization for the first time, and (3) we have 10x additional subjects over MUSHAC and 100x over SuperMUDI. Additionally, the data that form the basis of this challenge represent a difficult clinical scenario for harmonization and are part of a much larger twins study, which could provide rich context for continuing validation and extension of this challenge’s findings.

In the following, we introduce the challenge, describe the data and evaluation framework, and present baseline measures against which challenge submissions will be compared against. We end with a discussion on what we aim to investigate, and hope to learn from this community effort.

## 1.1 The Challenge

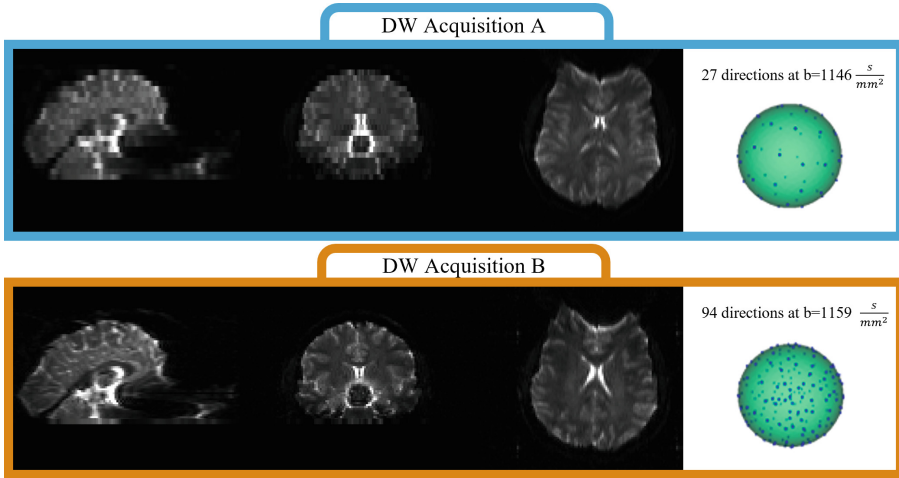
Participants are challenged to bridge acquisition disparities in scan-rescan DW-MRI data - using potentially preprocessing, super-resolution, and/or harmonization techniques. They are provided with a T1-weighted MRI and two DW-MRI scans for a cohort of 78 training and 25 testing patients. The core differences between the two acquisitions are (1) spatial resolution ( $1.8 \times 1.8 \times 5 \text{ mm}^3$  vs.  $1.8 \times 1.8 \times 2 \text{ mm}^3$ ) and (2) number of directions collected (27 vs. 94). These differences bias and confound three major groups of diffusion analysis: bundle microstructure, bundle macrostructure, and complex network measures (Fig. 1) [11, 17, 20, 21]. A successful challenge algorithm will minimize protocol differences in all three analyses.



**Fig. 1.** Acquisition differences affect microstructure measurements (FA map, left), macrostructure reconstructions (corticospinal tract shape, middle), and connectomics (whole brain connectome, right).

## 2 Data

The data that form the basis of this challenge represent a difficult clinical scenario for harmonization and are a subset of the Queensland Twin Imaging study [19]. The DW dataset consists of 25 matched testing and 78 training subjects scanned twice with two different acquisition protocols (Fig. 2). Testing and Training data used in this challenge are publicly available at [shared Box](#). Each subject has an anatomical 3D whole-brain T1-weighted image. The data subset is comprised of 45% females, ages  $25.3 \pm 1.8$  years. No subjects reported a history of significant head injury, neurological or psychiatric illness, or substance abuse or dependence, and no subjects had a first-degree relative with a psychiatric disorder. All subjects were right-handed as determined using 12 items from Annett’s Handedness Questionnaire [2]. Scanning was performed at the QIMR Berghofer Medical Research Institute on a 4 tesla Siemens Bruker Medspec scanner [19].



**Fig. 2.** Each subject was scanned using two protocols with different resolutions (left) and gradient directions (right). Image resolution and quality differences are apparent in visualizations of  $b_0$ -images ( $b = 0 \text{ s/mm}^2$ ).

## 2.1 Acquisition A

Acquisition A DW images were acquired using single-shot echo-planar imaging with a twice-refocused spin echo sequence. Imaging parameters were repetition/echo times of 6090/91.7 ms, field of view of 23 cm, and  $128 \times 128$  acquisition matrix. Each 3D volume consisted of 21 axial slices 5 mm thick with a 0.5 mm gap and  $1.8 \times 1.8 \text{ mm}^2$  in-plane resolution, total time = 3 min. Thirty images were acquired per subject: three with no diffusion sensitization ( $b = 0 \text{ s/mm}^2$ ) and 27 DW images ( $b = 1146 \text{ s/mm}^2$ ) with gradient directions uniformly distributed on the hemisphere.

## 2.2 Acquisition B

Acquisition B DW images were acquired using single-shot echo planar imaging (EPI) with a twice-refocused spin echo sequence. Imaging parameters were: 23cm FOV, TR/TE 6090/91.7 ms, with a  $128 \times 128$  acquisition matrix. Each 3D volume consisted of 55 2-mm thick axial slices with no gap and a  $1.79 \times 1.79 \text{ mm}^2$  in-plane resolution with total acquisition time = 14.2 min. 105 images were acquired per subject: 11 with no diffusion sensitization ( $b = 0 \text{ s/mm}^2$ ) and 94 DWI ( $b = 1159 \text{ s/mm}^2$ ) with gradient directions uniformly distributed on the hemisphere.

## 3 Testing Framework

Participants will submit 25 paired DW-MRI from the testing cohort. Submission processing includes: diffusion analysis of tensor fitting, orientation distribution

function (ODF) reconstruction, whole brain tractography, bundle segmentation, tractometry, bundle shape analysis, connectomics, and finally, complex network analysis. Code is available via a [public docker](#). Testing data are 2.9 GB and evaluation takes 9 h on a 64 GB RAM Macbook Pro.

Assessment will be performed to quantify the similarity of (1) bundle-specific microstructure measures, (2) macrostructural features of each pathway, and (3) complex network measures. Table 1 reports the baseline scores for each category.

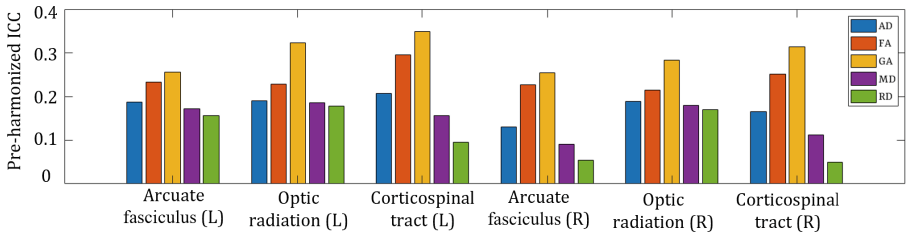
**Table 1.** Baseline scores for un-harmonized data.

Connectivity score	Microstructural score	Shape similarity score	Shape profile score
0.37	0.19	0.85	6.79

### 3.1 Bundle-Specific Microstructure

Microstructure measures of fractional anisotropy (FA), mean diffusivity (MD), geodesic anisotropy (GA), radial diffusivity (RD), and axial diffusivity (AD) are calculated for each of six pathways as the average DTI measure within each bundle: left/right Arcuate Fasciculus (AF), left/right Optic Radiations (OR), and left/right Corticospinal tract bundles (CST)

Ideally, DTI in these ROIs would be the same across scans for a single patient. However, Fig. 1 shows bundles are not consistent across acquisitions A and B. We use Intra-class Correlation Coefficient (ICC) to quantify reproducibility across acquisitions and bundles. ICC quantifies how well measurements of the same group resemble each other. The QIBA Technical Performance Working Group suggests using ICC to evaluate repeatability. The ICC is interpreted as follows: below 0.5 as “poor”, between 0.50 and 0.75 as “moderate”, between 0.75 and 0.90 as “good”, and above 0.90 as “excellent” [10]. We evaluate the repeatability of diffusion measures for scan-rescan of the same subject, for all 25 subjects in the testing cohort. Baseline results for ICC per bundle, before any preprocessing or harmonization solution has been applied, is reported in Fig. 3. We compute a single microstructural score that is the average ICC across bundles. Successful submissions will increase ICC and have a higher microstructural score than that reported in Table 1.



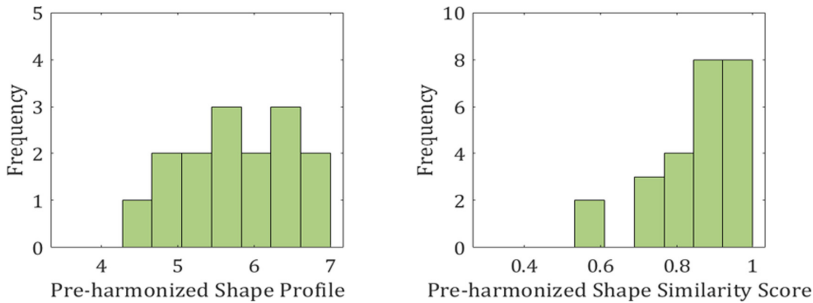
**Fig. 3.** ICC, computed across 25 A/B pairs, of bundle microstructural measures AD, FA, GA, MD, RD for 6 bundles. Successful submissions will improve consistency of microstructural measures and have higher ICC values.

### 3.2 Bundle-Specific Macrostructure

Using the same six bundles above, we use the BU $\text{N}$ dle ANalytics (BUAN) framework to compare the reconstructions created from each acquisitions' DW-MRI [5],[?].

BUAN provides bundle shape similarity scores to assess structural consistency among bundles. Bundle shape similarity is a streamline-based comparison approach that provides a single score between 0 (no match) and 1 (perfect match) between two bundles. Furthermore, we created bundle shape profiles using BundleWarp registration [4]. The bundle shape profile describes shape differences in bundles across the two acquisitions in terms of deformation magnitude generated by BundleWarp registration to match two bundles completely. Lower deformation magnitude implies fewer shape differences in two bundles, and higher deformation magnitude means a high number of deformations and/or transformations are required to align two bundles perfectly, hence having higher shape differences.

Bundle shapes should be consistent across scans of the same patient. Thus, we expect a successful submission will produce DW-MRI that has low bundle shape profiles and high shape similarity scores across acquisitions. The bundle shape profile and shape similarity scores are reported for 25 Test patients in Fig. 4. The final bundle-based score is the average across all 25 patients.



**Fig. 4.** BundleWarp macrostructure comparison measures, bundle shape profiles (left) and bundle shape similarity score (right), computed across acquisitions for all 25 test-set patients. Successful submissions will improve DW-MRI quality such that bundle shape similarities are higher and bundle shape profiles are lower.

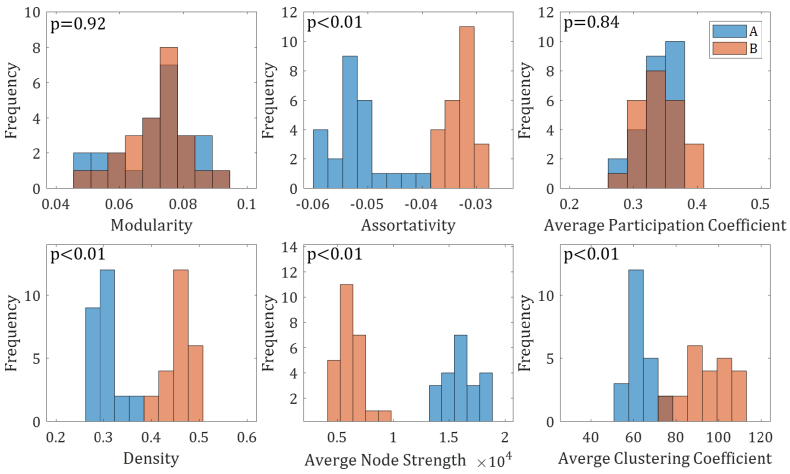
### 3.3 Connectome Measures

The last class of metrics that we derive are complex network measures computed on the connectome. To construct a connectome, we first reconstruct ODFs using the Constant Solid Angle (CSA) algorithm at a maximum spherical harmonic order of 6 [1]. Using the ODF and a white matter mask ( $FA > 0.1$ ), we perform whole-brain tractography using the EuDX [7] algorithm. The connectome is the result of segmenting and mapping the whole brain tractogram into brain

regions (nodes) and the streamlines connecting them (edges). For this challenge, tractograms are segmented based on the Desikan-Killiany atlas from FreeSurfer (version 7.2.0) with 87 cortical and subcortical regions [6].

Connectome measures are intended to characterize brain networks in a computationally simple yet meaningful manner [16]. In this challenge, we consider modularity, assortativity, average participation coefficient, density, average node strength, and average clustering coefficient. Modularity is the degree to which the network can be subdivided into clearly delineated subgroups and summarizes the community structure. Assortativity is a correlation coefficient between nodes of opposite ends of a link and reflects the network’s resilience. The participation coefficient is a measurement of the diversity of intermodular connections. Density is the fraction of present connections to total possible connections. Node strength is the sum of weights for edges connected to a given node. The clustering coefficient is the geometric mean associated with a node. We use the *scipy* (version 1.5.0) and *bctpy* (version 0.6.1) implementations of the Brain Connectivity Toolbox measure definitions [16].

A successful submission would produce DW-MRI with consistent complex network measures across acquisitions of the same patient. Figure 5 is a histogram report highlighting the significant baseline differences between acquisitions. We assess reproducibility across complex network measures with ICC. This ICC is the final connectivity score (Table 1).



**Fig. 5.** Histogram distributions for connectome measures derived from pre-harmonized A and B DWI acquisitions. t-test p-values for comparing means across the two acquisitions are reported in the top left corner.

## 4 Broader Contributions

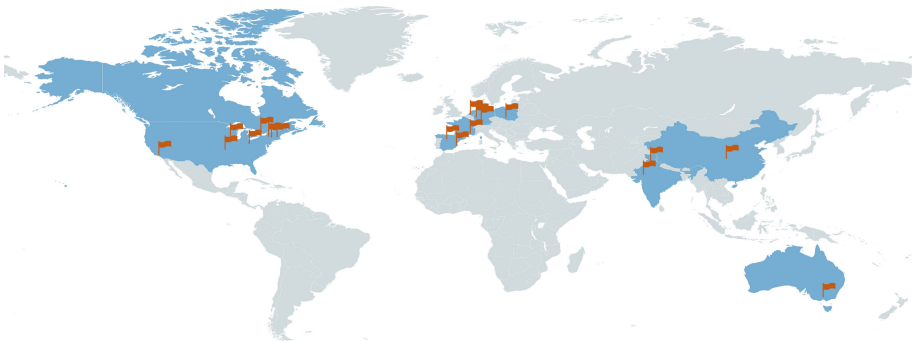
Data are increasingly coming from multi-center, multi-site, and multi-acquisition sources, and it is important to utilize these datasets to detect changes in

development [3,9,18], Alzheimer’s disease [12,14], and autism [8]. For this reason, harmonization is particularly important in DW-MRI so that bundles and connectomes are comparable, and we can study features from micro-scale to macro-scale. These features act as potential biomarkers for neurological diseases, and subtle, important changes can be overshadowed by un-harmonized biases.

This challenge gives us insight into the efficacy of diffusion harmonization methods that aim to make one site acquisition like another. Current examples include statistical and image-based methods, which have proven useful so far, but methods are continuously being developed and improved. This study is a benchmark that lets us define method successes and limitations. A successful submission in this challenge is one that overcomes the dramatic differences due to resolution and gradient directions. While this challenge tasks image-based methods of diffusion harmonization, i.e. making the signal from scanners similar, we do not specifically investigate statistical approaches which have become common in literature (ComBat, CovBat, NeuroCombat). As an extension of this challenge and all submissions, we plan to investigate the fidelity and robustness of statistical feature based harmonization methods. For example, we are not aware of these approaches being applied to features of bundles.

Beyond simple harmonization, this challenge also acts as a super-resolution task. The task of super resolution is simply to perform image processing that results in an image with information captured at a higher resolution than it was acquired at. This method is important in tractography to make data isotropic, and is more critical as we try to investigate smaller structures in the brain. A successful submission in this challenge will necessitate super-resolving the low resolution dataset to generate a higher, isotropic resolution dataset that closely matches signal actually acquired at a higher spatial resolution.

Finally, preprocessing is necessary to remove effects and biases and improve SNR. For example, preprocessing mitigates motion, susceptibility and eddy current distortions - a necessary step for robust, reproducible measurements. Because these data have different acquisitions and, therefore, different artifacts and distortions, this is a study on preprocessing techniques that minimize differences due to imaging artifacts.



**Fig. 6.** Twenty teams from across the world have registered to participate in the Quant-Conn challenge. This map visualization was made with mapchart.com.

We expect participants (Fig. 6) to submit a range of methods such as explicit signal harmonization, resolution adjustments, and machine learning solutions.

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