Evaluation of Reproducibility of Diffusion Tensor Imaging in the Brachial Plexus at 3.0 T

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**Objective:** The aim of this study was to evaluate the reproducibility of 3 T magnetic resonance imaging diffusion tensor imaging (DTI) of the brachial plexus in healthy subjects.

**Methods:** Ten healthy volunteers were included, and morphological and DTI sequences of the nerve roots of the brachial plexus from C5 to T1 of both sides were repeatedly acquired on a 3 T magnetic resonance system (MAGNETOM Skyra; Siemens Healthcare, Erlangen, Germany). A prototype diffusion-weighted single-shot echo-planar imaging sequence-enabling slice-specific shim adjustments was performed with b-values of 0 and 800 s/mm² in 30 gradient directions, resulting in an acquisition time of about 6 minutes each in axial orientation. Between scans, subjects were moved and repositioned in the scanner, coils were reinserted, and new localizers were acquired. Image analysis was performed using MITK Diffusion software toolkit. Two independent readers performed diffusion data postprocessing, and regions of interest (ROIs) were set on the proximal postganglionic trunk at each spinal level, bilaterally to obtain values for fractional anisotropy (FA) and mean diffusivity (MD). Interreader and intrareader agreement as well as test-retest reproducibility of DTI metrics were assessed.

**Results:** Intraclass correlation coefficients (ICCs) for interreader and intrareader agreement did not differ significantly between measurements for FA and MD. In particular, ICCs for interreader agreement of FA ranged from 0.741 to 0.961 and that of MD ranged from 0.802 to 0.998, and ICCs for intrareader agreement of FA ranged from 0.759 to 0.949 and that of MD ranged from 0.796 to 0.998. The test-retest reproducibility of DTI metrics showed an overall moderate to strong correlation (r > 0.707), with few minor exceptions, for both FA and MD values.

**Conclusions:** Diffusion tensor imaging metrics in the brachial plexus are reproducible. Future applications of DTI for a possible clinical use should be further investigated.

**Key Words:** MRN, DTI peripheral nerves, brachial plexus

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**TECHNICAL NOTE**

**Study Subjects**

Institutional ethics board approval and written informed consent of all volunteers were obtained. Ten healthy volunteers (mean age, 30.6 ± 5.3 years; range, 23–41 years), 6 women (mean age, 28.6 ± 5.9 years; 41 years), 6 women (mean age, 28.6 ± 5.9 years; range, 23–41 years), 6 women (mean age, 28.6 ± 5.9 years; range, 23–41 years), 6 women (mean age, 28.6 ± 5.9 years; range, 23–41 years), 6 women (mean age, 28.6 ± 5.9 years; range, 23–41 years)
Reproducibility of DTI in the Brachial Plexus

In-plane resolution, mm
Slice thickness, mm
No. slices
Slice thickness, mm
Pixel bandwidth, Hz/px
Acquisition time, min:s

Sequence Parameters

<table>
<thead>
<tr>
<th></th>
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<th>SPACE STIR</th>
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<tr>
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<tr>
<td>Acquisition time, min:s</td>
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</table>

DTI indicates diffusion tensor imaging (used here: prototype diffusion-weighted ss-EPI sequence enabling slice-specific shim adjustments); SPACE, sampling perfection with application of optimized contrasts using different flip angle evolution; STIR, short tau inversion recovery; TR, repetition time; TE, echo time; FOV, field of view.

range, 23–41 years) and 4 men (mean age, 33.3 ± 3.0 years; range, 28–37 years), were recruited. Exclusion criteria were general contraindications to magnetic resonance (ie, pacemaker, claustrophobia), age younger than 18 years, history of findings related to nerve abnormalities (ie, upper extremity pain, paresthesia, or hypesthesia), history of cervical spine abnormalities, or prior surgery of the cervical spine or the brachial plexus.

Magnetic Resonance Imaging

Morphological and DTI sequences of the brachial plexus of both sides were acquired on a 3.0 T magnetic resonance system (MAGNETOM Skyra; Siemens Healthcare, Erlangen, Germany) using a commercially available 64-channel head-neck coil and appropriate elements of both an 18-channel body array and a 32-channel spine array between May and October 2015. An isotropic T2-weighted sampling perfection with application of optimized contrasts using different flip angle evolution (SPACE) sequence with short tau inversion recovery (STIR) fat suppression in coronal orientation was applied for better anatomical orientation with the following sequence parameters: repetition time, 3500 milliseconds; echo time, 166 milliseconds; voxel size, 0.8 × 0.8 mm; slice thickness, 0.8 mm; number of slices, 144; field of view (FOV), 260 × 260 mm; receive bandwidth, 454 Hz/px. A prototype diffusion-weighted single-shot echo-planar imaging (ss-EPI) sequence enabling slice-specific shim adjustments with b-values of 0 and 800 s/mm² in 30 gradient directions was applied, acquiring voxels with an isotropic dimension of 1.9 mm.¹³,¹⁴ Total acquisition time corresponded to 21 minutes. Pulse sequence-specific DTI parameters are summarized in Table 1.

Slice-specific shim adjustments facilitate the acquisition of echo-planar images with decent image quality in the neck region. Because of its intrinsically low bandwidth along the phase-encoding direction, EPI quality suffers from the presence of residual fat signal as well as from local, subject-induced B0 field inhomogeneities. For multislice acquisitions, established shim procedures enable partial mitigation of these degradations only: this is due to the fact that a single, static setting of first- and, if applicable, higher-order shim fields that satisfies average optimization criteria gets applied throughout the measurement for the complete set of slices. The ss-EPI sequence prototype used in this study supports localized, slice-specific optimizations and dynamically switches assigned shim settings synchronously with the acquisition of each slice.¹³,¹⁴

After the initial scan, each subject underwent a second separate MRI examination on the same day in the same scanner. The second scanning session contained the identical DTI sequence of the initial session. Between the 2 scans, volunteers were moved and repositioned in the scanner, coils were replaced, and new localizers were acquired (Fig. 1).

Image Analysis

All 3-dimensional data sets were analyzed by 2 independent readers (reader 1, M.J.H., research fellow in musculoskeletal radiology with 2 years' training in neuroradiology; reader 2, A.M., clinical fellow in musculoskeletal radiology with a PhD in neuroimaging, both with experience in diffusion data postprocessing and peripheral nerve segmentation) according to the sequential scheme reported in Figure 1. The open-source software MITK Diffusion (release 2015.05; www.mitk.org) was used for postprocessing of raw data and to perform diffusion tensor maps for FA and MD estimation for each subject.¹⁵ Anisotropy and MD values were obtained as follows: at all levels from C5 to T1, nerves roots in both sides were identified on the SPACE STIR sequence and on the TRACE image obtained from postprocessing of DTI data. Subsequently, on the TRACE-weighted images, circular regions of interest (ROIs) with a fixed area of 11 mm² were set on the proximal postganglionic, supravacuicular trunks of both sides at all levels of the brachial plexus. Regions of interest were

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FIGURE 1. Flow chart of study procedures. Participants underwent 2 magnetic resonance scans with repositioning between scans. For reproducibility of measurements, independent readouts were performed by 2 readers after the first scan and 6 weeks later by 1 reader. For test-retest reproducibility, 1 reader performed an additional measurement of DTI metrics. Figure 1 can be viewed online in color at www.investigativeradiology.com.
meticulously positioned within the brachial plexus at the level of the trunks to minimize partial volume effects (Fig. 2). Subsequently, the software automatically calculated corresponding FA and MD values. The same procedure was also performed to obtain FA and MD values of spinal cord at C7 level.

Statistical Analysis
All statistical analyses were performed using SPSS (release 22.0; SPSS Inc, Chicago, IL). Descriptive statistics was performed, and mean FA and MD values were obtained from the analysis of reader 1 after the first readout and from reader 2. For the assessment of interreader and intrareader agreement of measurements, intraclass correlation coefficients (ICCs) for mean FA and for mean MD values of each level of the brachial plexus from C5 to T1 for both sides and the spinal cord at the level of C7 were computed. To calculate ICCs between independent readers, 2-way random effects models were applied. Interreader and intrareader agreement was considered excellent for values greater than 0.75, values between 0.40 and 0.75 reported fair to good reliability, and values below 0.40 indicated poor agreement. For reproducibility analysis, test-retest Pearson correlation coefficients were calculated for FA and MD and interpreted as follows: correlation was considered weak when \( r \) was less than 0.3, moderate when \( r \) was between 0.3 and 0.7, and strong when \( r \) was greater than 0.7. Results were referred to as statistically significant when \( P \) value is equal to 0.025. Statistical tests were Bonferroni corrected for multiple comparisons, where applicable.

RESULTS
Morphological and DTI images were successfully acquired in all healthy volunteers. In all T2 SPACE STIR images and in all TRACE images of all subjects, the supraclavicular brachial plexus was completely delineated and the course of nerve structure was depicted without discontinuity (Fig. 3). Mean FA and MD values and the detailed results from ICC analysis and Pearson correlation analyses are demonstrated in Table 2.

Interreader and Intrareader Agreement
An excellent interreader and intrareader agreement (ICC > 0.756 and ICC > 0.759, respectively) was observed for both FA and MD values at all levels, except for the FA value at C5 level on the left side (ICC = 0.741). The highest ICC for interreader agreement with 0.961 (\( P < 0.001 \)) for FA was noted at the level of C6 on the left side, and that for intrareader agreement with 0.949 (\( P < 0.001 \)) for FA was noted at the level of T1 left. The lowest interreader and intrareader agreement for FA was found at the level of C5 left with an ICC of 0.741 (\( P = 0.025 \)) and at the level of C5 right with an ICC of 0.759 (\( P = 0.023 \)), respectively. For MD, the highest ICC for interreader and intrareader was found at the level of C5 on the right side and was 0.998 (\( P < 0.001 \)) for both. The lowest interreader correlation with an ICC of 0.796 (\( P = 0.13 \)) and

FIGURE 2. Measurement of diffusion metrics with MITK Diffusion toolkit at the level of C6 on the right supraclavicular brachial plexus in a 36-year-old man. Reference lines on axial (A) and sagittal (B) reconstructions and on coronal (C) TRACE images of the DTI magnetic resonance scan were used for ROI placement in the trunks of the supraclavicular brachial plexus of both sides. Figure 2 can be viewed online in color at www.investigativeradiology.com.

FIGURE 3. Morphological correlation and results for repeated DTI scans in a 27-year-old healthy female volunteer. Panel A, coronal SPACE STIR of the brachial plexus for anatomical orientation; panel B, coronal maximum intensity projection of the TRACE image of the DTI magnetic resonance from scan 1 (slab thickness, 37.0 mm); panel C, coronal maximum intensity projection of the TRACE image of the DTI magnetic resonance from scan 2 (slab thickness, 37.0 mm). Brachial plexus anatomy is repeatedly and clearly depicted in scan 1 (B) and scan 2 (C) in accordance with the SPACE STIR image (A) as reference image.
the lowest intrareader with an ICC of 0.802 (P = 0.12) for MD were found at the level of T1 at the right side.

### Reproducibility

In the analysis of test-retest reproducibility of brachial plexus DTI parameters, an overall strong correlation was found (r > 0.707). Indeed, FA values demonstrated to be reproducible without significant differences between the independent readouts and showed throughout positive correlation between measurements of test and retest at most of the levels. Fractional anisotropy values were linearly but not significantly correlated only at the levels C5 of both sides and at C8 left and T1 left. Similar results were found for MD, with a nonsignificant but still linear correlation, only at the level of T1 on the right side (r = 0.598). Otherwise, all test-retest showed moderate to excellent correlation with values ranging from 0.361 (C5 right side) to 0.954 (C6 left side). Mean diffusivity Pearson correlation coefficients ranged from moderate to strong correlation with 0.598 (P = 0.09) for T1 right and with 0.986 (P < 0.001) for C5 right.

### Spinal Cord Measurements

Evaluation of spinal cord at C7 level resulted in excellent ICCs for interreader correlation with 0.866 (P = 0.03) and for intrareader correlation with 0.924 (P < 0.001) for FA, and, respectively, with 0.924 (P < 0.001) and with 0.914 (P < 0.001) for MD. Test and retest demonstrated a strong linear correlation for FA (Pearson r = 0.794; P = 0.06) and strong linear correlation for MD (Pearson r = 0.933; P < 0.001).

### DISCUSSION

In the current study, the reproducibility of quantitative DTI of the brachial plexus was assessed with a dedicated pulse sequence at 3 T.
Nerve course in the brachial plexus was clearly depicted in all anatomic and diffusion sequences for subsequent measurements. Intraobserver, interobserver, and test-retest showed excellent reproducibility of FA and MD values in almost all levels of the trunks of the brachial plexus from C5 to T1 of both sides.

In comparison to prior studies, which aimed to assess feasibility and reproducibility of DTI measurements in the brachial plexus, this study is the only one in which test-retest MRI scans were conducted, including separate and independent postprocessing procedures for each scan, to comprehensively assess reproducibility. In addition, a novel imaging approach consisting of a conventional single-shot diffusion-weighted EPI sequence in combination with slice-selective optimization of the magnetic field homogeneity was used to reduce geometric distortions and improve fat suppression. Other approaches to reduce geometrical distortions in diffusion-weighted MRI include reduced FOV\textsuperscript{18} imaging and readout-segmented acquisitions.\textsuperscript{19} Compared with reduced FOV imaging, the sequence used in this study resulted in higher SNR. While readout-segmented EPI allows high in-plane resolutions, resulting measurement times of this multishot approach prevent its use for clinical DTI examinations requiring many diffusion encoding directions.

The decisive operator-dependent step in this study was the placement of ROIs in cross-sectional images for subsequent ROI-based data analysis. A fixed ROI diameter smaller than the nerve cross-sectional diameter restricted the contamination of DTI metrics from surrounding tissue with different diffusion characteristics. Provided that all ROIs were set within the nerve and taking into account the small nerve caliber, ROI data analysis for a test magnetic resonance scan was based only on a choice of few voxels—if not even identical voxels. Apart from an optimized setting in the trial with a dedicated design of the diffusion imaging protocol, state-to-the-art software and hardware, this might be an important factor for the overall good results for interobserver, intrarater, and test-retest according to ICCs and Pearson correlation coefficients. For an assessment of relatively novel DTI of the brachial plexus, better established DTI of the spinal cord was conducted additionally at level of C7. A greater diameter of the spinal cord with a high directionality of nerve fibers is expected to result in a signal of nerve tissue not lower than the one to be yielded in the brachial plexus. In the central nervous system, it has been suggested that axonal diameter, density, and myelination have an influence on the measurement of diffusion parameters.\textsuperscript{20,21} Beside this, DTI measurements in the spinal cord previously have been shown of high reproducibility.\textsuperscript{22,23} In comparison to DTI measurements of the spinal cord, ICCs for interrater and intrarater DTI data of the brachial plexus at C7 for both sides showed only slightly lower ICCs for MD, but even better ICCs for FA values. Test and retest results were highly correlated for the spinal cord as well as for the brachial plexus. Still, DTI of the brachial plexus has an inherent SNR dilemma: on one hand, relatively small caliber of the nerves only on a few voxel designs with smaller in-plane resolution than the cross-sectional diameter of the nerve itself to avoid partial volume effects from surrounding structures. Small voxel size, on the other hand, limits the signal that can be derived, resulting in unfavorable SNR. In this study, we used small isotropic voxel for a better adaption to nerve anatomy because some trunks leave the spinal cord in a rather steep angle to change direction again when passing behind the clavicle. When investigating only parts of the brachial plexus (other than in the brain, where crossing of nerve fibers can influence the precision of measurement of DTI metrics), anisotropic voxels, which allow for higher voxel volume, might be an alternative to increase nerve signal.\textsuperscript{24,25}

Limitations

Certain limitations in the study design have to be acknowledged. With 10 healthy volunteers, the number of subjects was small. Nevertheless, all data revealed consistency with low standard deviations. Furthermore, no symptomatic participants were included in this study. However, the aim of this study was to address the issue of reproducibility of measurement of DTI metrics before proceeding to promising clinical applications. In addition, the impact of vendor-specific differences in equipment on reproducibility on DTI parameter measurement was not assessed in this study. Previously, an investigation on the influence of different hardware in DTI measurement of peripheral nerves has revealed significant differences in absolute values of derived DTI parameters between vendors. However, due to consistently small standard deviations of absolute DTI values, no impact on larger clinical group studies with substantial DTI changes was expected.\textsuperscript{26} Regarding interrater and interrater agreement between software packages, no substantial contribution to variance of software in DTI measurements was assumed.\textsuperscript{27}

CONCLUSIONS

This study demonstrates that DTI metrics, FA, and MD in the brachial plexus are highly reproducible. Promising applications of DTI for a possible, future clinical use comprise a wide range of plexopathies from neurodegenerative diseases, tumor-like conditions, inflammation, and compression syndromes to trauma. Further studies are to be conducted to test if DTI of the brachial plexus can be of additional diagnostic value beyond traditional MRN.

REFERENCES

14. Feiweier T, Fischer D, Jeschke H, et al. Method for operating an MRI system, state-to-the-art software and hardware, this might be an important factor for the overall good results for interobserver, intrarater, and test-retest according to ICCs and Pearson correlation coefficients. For an assessment of relatively novel DTI of the brachial plexus, better established DTI of the spinal cord was conducted additionally at level of C7. A greater diameter of the spinal cord with a high directionality of nerve fibers is expected to result in a signal of nerve tissue not lower than the one to be yielded in the brachial plexus. In the central nervous system, it has been suggested that axonal diameter, density, and myelination have an influence on the measurement of diffusion parameters.20,21 Beside this, DTI measurements in the spinal cord previously have been shown of high reproducibility.22,23 In comparison to DTI measurements of the spinal cord, ICCs for interrater and intrarater DTI data of the brachial plexus at C7 for both sides showed only slightly lower ICCs for MD, but even better ICCs for FA values. Test and retest results were highly correlated for the spinal cord as well as for the brachial plexus. Still, DTI of the brachial plexus has an inherent SNR dilemma: on one hand, relatively small caliber of the nerves only on a few voxel designs with smaller in-plane resolution than the cross-sectional diameter of the nerve itself to avoid partial volume effects from surrounding structures. Small voxel size, on the other hand, limits the signal that can be derived, resulting in unfavorable SNR. In this study, we used small isotropic voxel for a better adaption to nerve anatomy because some trunks leave the spinal cord in a rather steep angle to change direction again when passing behind the clavicle. When investigating only parts of the brachial plexus (other than in the brain, where crossing of nerve fibers can influence the precision of measurement of DTI metrics), anisotropic voxels, which allow for higher voxel volume, might be an alternative to increase nerve signal.24,25

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