Diffusion tensor imaging of the median nerve at 3.0T: normative diffusion values in different age groups

Poster No.: C-1200
Congress: ECR 2011
Type: Scientific Paper
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Keywords: Musculoskeletal soft tissue, Neuroradiology peripheral nerve, MR, MR-Diffusion/Perfusion
DOI: 10.1594/ecr2011/C-1200

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**Purpose**

An increasing number of articles about diffusion tensor imaging of peripheral nerves has recently been published. (1-6)

DTI may play a role in the detection and quantification of peripheral neuropathies, e.g. compressive neuropathy of the median nerve at the carpal tunnel (carpal tunnel syndrome). (3-5)

However, normative diffusion values of the median nerve such as fractional anisotropy (FA) and apparent diffusion coefficient (ADC) have never been systematically evaluated in order to differentiate physiologic from pathologic diffusion values of the nerve.

Thus, the aim of this study was to determine normative diffusion values of the median nerve at 3 Tesla in different age groups and both sexes.
Methods and Materials

This is a local ethical board-approved study with written informed consent from 45 healthy volunteers;

Volunteers were divided into three age-groups with 10 women and 5 men each: 18-34 years (group I), 35-49 years (group II) and 50-75 years (group III).

All volunteers underwent DTI of their dominant, right wrist at 3.0 Tesla (Achieva, Phillips, Best, The Netherlands) using a dedicated 8-channel wrist coil and a single-shot echo-planar-imaging sequence (TR/TE 10123/40ms; b-value 1200s/mm2).

Nerve cross-sectional area (CSA), FA and ADC of the median nerve were determined by two readers at three different localisations: at the level of the distal radio-ulnar joint, the pisiform and hamate bone.

MR-Imaging:

Axial T1-weighted turbo spin echo (TSE) anatomic reference images were acquired in a first step (see Figure 1a).

(Repetition time/ echo time (TR/TE), 636/21 ms; matrix size, 400 x 264 mm; field-of-view (FoV), 120 x 80 mm; voxel size, 0,3 x 0,3 x 4 mm (slice thickness 4 mm, reconstructed voxel size 0,15 x 0,15 x 4 mm); number of slices, 25; turbo spin echo (TSE) factor, 3; number of signal averages (NSA), 1; Sense factor in ap-direction, 2, acquisition-time, 4:38 min)

Secondly, DTI acquisitions were performed and consisted of a single shot echo planar imaging (EPI) sequence with a b-value of 1200s/mm2 and 15 gradient encoding directions.

(TR/TE 10123/40 ms; b-value, 1200 s/mm2; matrix size, 100 x 82 mm; FoV, 120 x 100 mm; voxel size, 1,2 x 1,2 x 4 mm (slice thickness 4 mm; reconstructed voxel size 0,54 x 0,54 x 4 mm); number of gradients, 15; number of slices, 25; NSA 2; fat suppression, SPAIR; EPI factor 45; Sense factor in ap - direction 2; acquisition time, 6:06 min).

MR-Post-Processing:
All MR-images were then loaded to a separate workstation and post-processed by two different readers using dedicated DTI-software (Phillips Achieva Release 3.2.1.0.).

Both readers were trained by an experienced radiologist (8 years in musculoskeletal imaging) prior to their read-out using test-data assuring comparable and standardized post-processing.

First semiautomatic FA- and ADC-maps were generated automatically by the software using the DTI source-acquisitions.

(see Figure 1b and 1c)

In a second step, three standard localisations of the carpal tunnel were chosen on axial T1-weighted images for the DTI measurements of the median nerve:

1. distal radio-ulnar joint
2. pisiform and
3. hamate bone.

A region of interest (ROI) was drawn manually around the median nerve on all three localisations yielding nerve cross sectional area (CSA). Care was taken to include nerve tissue only and exclude surrounding fat, tendons or any other than nerve tissue.

ROIs were then copied from the anatomical slices (Figure 1a) to the identical positions and slices of the corresponding FA- (Figure 1b) and ADC-maps (Figure 1c).

CSA, mean FA- und ADC-values of the ROIs were then generated automatically by the software and used for data-analysis.

**Statistical Analysis:**

All statistical analysis were performed using dedicated software (SPSS® 18.0; SPSS Inc., Chicago, Ill).

A p-value of p < 0.05 was considered statistically significant.

One way analysis of variance (ANOVA) of different population means were performed, using the Bonferroni procedure for multiple post-hoc comparisons. Data between female and male volunteers were compared using unpaired t-tests.
In order to assess inter-reader variability, intra-class correlation coefficients (ICC) were calculated.

An ICC = 0 was considered poor, ICC = 0.21-0.60 fair to moderate, ICC = 0.61-0.80 substantial and >0.80 almost perfect inter-reader agreement.
Fig. 0: 1a) Anatomic slice at level of hamate bone, hamulus (asterisk) and region of interest (ROI) drawn around median nerve (arrow); 1b) FA-map and 1c) ADC-map at same slice location with copied ROI from anatomic slice.

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Results

The Intra-class-correlation coefficients (ICCs) for FA, ADC and CSA were 0.91, 0.94 and 0.62 respectively, showing almost perfect inter-reader agreement for FA and ADC and moderate to substantial agreement for CSA.

CSA-Analysis:

The mean CSA of the median nerve for all volunteers and all localisations was 11.5 ± 3.5 mm² (female: 10.6 ± 3.1 mm², male: 13.2 ± 3.6 mm²).

There was a significant over-all difference for CSA of the median nerve between female and male wrists (p<0.000).

FA-Analysis:

In the youngest age-group I mean FA of all localisations was 0.59 ± 0.09, with 0.58 ± 0.09 for female and 0.59 ± 0.10 for male.

In age-group II mean FA of all localisations was FA 0.52 ± 0.09, with 0.53 ± 0.09 for female and 0.51 ± 0.08 for male.

In the oldest age-group III of volunteers mean FA of all localisations was found to be 0.48 ± 0.08, with 0.47 ± 0.09 for female and 0.50 ± 0.06 for male respectively.

Thus, a significant decrease of the mean FA (p<0.000) with increasing age but no significant differences between both sexes were found (p = 0.104) (see Figure 2).

ADC-Analysis:

Mean ADC of all localisations in the youngest age-group I was 986.7 ± 179.9 x10-6 mm²/s, with 975.8 ± 171.8 x10-6 mm²/s for female volunteers and 1008.4 ± 167.6 x10-6 mm²/s for male volunteers, respectively.

In age-group II mean ADC of all localisations was 1063.1 ± 172.3 x10-6 mm²/s, with 1062.2 ± 173.2 x10-6 mm²/s for female volunteers and 1064.9 ± 171.1 x10-6 mm²/s for male volunteers.

Mean ADC of all localisations in the oldest age-group III was 1136.0 ± 160.9 x10-6 mm²/s, with 1121.2 ± 158.2 x10-6 mm²/s for female and 1165.9 ± 162.8 x10-6 mm²/s for male participants.
Thus the mean ADC of all localisations increased significantly with age (p<0.000) but did not differ significantly between female and male (p = 0.10) (see Figure 3).

A significant decrease of the FA of the median nerve was found from proximal to distal along the carpal tunnel (p<0.000) with a simultaneous increase of the mean ADC at the level of the pisiform, but a drop at the level of the hamate (p<0.000).

Mean CSA increased significantly (p<0.001) from the level of the distal radio-ulnar joint (9.7 ± 2.4 mm²) to the more distal level of the hamate (12.7 ± 3.6 mm²) (see Figure 4).
Fig. 0: 1a) Anatomic slice at level of hamate bone, hamulus (asterisk) and region of interest (ROI) drawn around median nerve (arrow); 1b) FA-map and 1c) ADC-map at same slice location with copied ROI from anatomic slice.

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Fig. 0: A significant decrease of the mean FA of all localisations with increasing age was seen, but no differences between both sexes were found ($p = 0.104$).

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Fig. 0: The mean ADC of all localisations increased significantly with age but no differences between both sexes were seen.

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**Fig. 0:** Mean CSA, FA and ADC at three different localisations of the wrist. Note significant decrease of the FA of the median nerve from proximal to distal along the carpal tunnel with inverse trend for ADC.

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Conclusion

To the best of our knowledge there is no study, where normative diffusion values of the median nerve at 3 Tesla have been assessed in a systematic and prospective study design and in a large study population of 45 healthy volunteers.

We could show a decrease of the mean FA and an increase of the mean ADC of the median nerve at the wrist with age, but no significant differences between men and women, except for CSA.

The latter finding is rather intuitive, given the different physiognomy of male vs. female individuals.

Further, the FA of the median nerve at the wrist decreased significantly from a proximal (distal radio-ulnar joint) to a more distal localisation (hamate bone).

The ADC increased from the most proximal (distal radio-ulnar joint) to the more distal location of the pisiform - where it showed the highest of all localisations - to further decrease again at the level of the hamate bone.

Crossing fibers within one voxel, changing nerve diameter with a lower signal-to-noise ratio (SNR) and the inclusion of tissue other than nerve fibers might alter diffusion characteristics and eventually lead to a decrease in FA and increase in ADC respectively. Changes of the FA- and ADC-values at different levels of the carpal tunnel may warrant further investigation.

Our normative values may serve as reference standards for DTI measurements of the median nerve at 3 Tesla and may help differentiate physiologic, age-related changes from pathologic conditions in peripheral neuropathies, e.g. carpal tunnel syndrome.
References


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