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Post-mortem diffusion MRI of the cervical spine and its nerve roots

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ABSTRACT

Purpose: The aim of this work is to examine the architectural configuration and the microstructural substrate of the cervical spine and its nerve roots with post-mortem (PM) diffusion tensor imaging (DTI) in non-fixed subjects and to compare these findings with histology.

Methods: Magnetic resonance imaging (MRI) data were acquired on a 1.5 T MRI scanner in five non-fixed non-trauma deaths. Two different areas were evaluated: 1) *the cervical spinal cord and ventral and dorsal nerve roots* with a "high in-plane" DTI and a multi-echo fast field echo protocol, and 2) *the cervical peripheral nerves* with an "isotropic" DTI and a 3D turbo spin echo protocol. Histology samples were obtained matching the anatomical level of the slices of the 'high in-plane' DTI protocol.

Results: We were able to show detailed reconstructions of the dorsal and ventral nerve roots with the 'high in-plane' protocol and identified a low fractional anisotropy (FA = 0.30 ± 0.08) in the grey matter and a high FA (0.51 ± 0.13) in the white matter. Both grey and white matter configurations correlated with the anatomical MRI, the diffusion MRI, and with the histological sections. Using the 'isotropic' DTI protocol, it was feasible to reconstruct the spinal cord, cervical nerves, and nerve roots in all PM subjects.

Conclusion: We were able to generate detailed architectural configurations of the ventral and dorsal nerve roots. Anatomical and diffusion MR scans showed good qualitative agreement with histology. We believe that PMDTI will be helpful in the assessment of head and neck injuries in a forensic setting.

1. Introduction

In forensic sciences the employment of imaging techniques such as magnetic resonance imaging (MRI) has been proven to be very effective in the identification of tissue trauma and therefore the use of different MRI techniques has increased in forensic examinations [1–3]. Examinations of the spinal cord and the peripheral nerves in the cervical area are often challenging, since nervous tissue can be difficult to dissect. Those procedures are of particular interest in cases such as traffic accidents, hangings, but also in other cases with possible spinal cord injuries [4]. This is especially the case where head and neck trauma are suspected, but no external sign of violence is present, such as, for example, after violent shaking of babies. As such, it is important to have methods that can accurately image nerve tissue in the region of the neck [5,6]. MRI has been proven useful in the identification of the cervical spinal cord injuries in vivo, but its potential value in post-mortem (PM) examinations in this region is unknown [7,8].

A sensitive method for evaluation of nervous tissue is diffusion MRI. Diffusion tensor imaging (DTI) is an MRI technique that allows for the quantification of diffusion of water molecules in tissue [9,10]. In nervous tissue, diffusion is larger along the nerve (axial diffusivity; AD), than perpendicular to the nerve (radial diffusivity; RD) [10–12]. In vivo, DTI has already been used to investigate the cervical spine and peripheral nerves [13,14]. Furthermore, it has been shown that DTI is reproducible in reconstructing the architecture of the lumbar and sacral nerves using fiber tractography (FT) and also in calculating diffusion properties in PM subjects within one scan session and over days [15]. However, exactly how DTI should be applied in the cervical spinal cord PM to distinguish between grey and white matter and how detailed nervous structures can be displayed remains to be investigated. As previously shown, validation with histology is needed to assess the added value of DTI for investigating peripheral nervous tissue [16]. Therefore, the aim of this work is to examine the architectural configuration and the microstructural substrate of the cervical spine and its

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Table 1
Subject information.

Identification number	Age	Sex	Approximate number of days between death and scan	History	Cause of death
1	36	Male	4	Drug addict	Acute myocardial infarction
2	70	Male	4	Dead 3 days after surgery	Pneumonia
3	25	Male	4	Drug addict	Overdose
4	90	Male	4	Surgery for hip fracture 9 days	Ischemic heart disease
5	33	Male	5	Drug addict	Overdose

nerve roots with PMDTI and compare it to histological dissection in non-fixed subjects.

2. Materials and methods

2.1. Subjects

Five non-fixed PM subjects with expected normal anatomy of the cervical spine were included; five men with a mean age of 51 years (range 25–90 years) all non-trauma deaths. All subjects were cooled in the morgue at 4 °C before and after autopsy without fixative solution preparation. MRI was performed 4–5 days after death. Additional subject information is listed in Table 1.

2.2. Data acquisition

All subjects were scanned at the level of the C4-C8 on a 1.5 T MR scanner (Ingenia; Philips Healthcare, Best, The Netherlands) using a head-neck neurovascular 16-channel surface coil. Two different areas in the cervical spine were evaluated: 1) *the cervical spinal cord and ventral and dorsal nerve roots* (C5-C7) with a "high in-plane" resolution DTI and a T2*-weighted multi echo fast field echo (mFFE) protocol, and 2) *the cervical peripheral nerves* (C4-C8) with an "isotropic" resolution DTI and a 3D turbo spin echo (TSE) protocol. An overview of the scan parameters is given in Table 2. Temperature of the body was measured before and after each MRI session as earlier described [15].

2.3. Data analysis

Before processing, all data was visually inspected for artifacts and overall image quality [10]. Next, the diffusion MRI toolbox *ExploreDTI* (www.ExploreDTI.com) [17] was used to process the DTI data. DTI datasets from both scan protocols were processed identically which comprised the following steps. First, the data were corrected for eddy current induced distortions [18]. Second, diffusion tensors were fitted using the iteratively weighted linear regression procedure [19]. Third, to reconstruct the fiber pathways a deterministic FT approach was used with the following settings [20]: step size of 1 mm, a fractional anisotropy (FA) threshold of 0.15, minimum fiber length of 10 mm, and an angle deviation of 30° per integration step. Average values of the diffusion parameters for both DTI datasets were determined using manually drawn regions of interest (ROIs) and tract based analysis.

Table 2
MRI acquisition parameters.

Protocol name	DTI isotropic	DTI in plane	mFFE
Plane	Coronal	Axial	Axial
TE (ms)	89	117	TE1 = 8.7 (ΔTE = 10.2)
TR (ms)	12882	2923	700
NSA (number of acquisitions)	2	20	2
Field of view (mm^2)	280 × 120	240 × 60	160 × 160
Acquisition matrix	112 × 47	240 × 59	248 × 246
Voxel size (mm^3)	2.5 × 2.5 × 2.5	1.0 × 1.0 × 5.0	0.29 × 0.29 × 5.0
Slices	30	10	17
b-value (s/mm^2)	2000	2000	–
Number of gradient directions	15	15	–
Acquisition time	45:44	15:38	5:47

2.4. The cervical spinal cord and ventral and dorsal nerve roots (C5-C7)

More specifically for the *cervical spinal cord and ventral and dorsal nerve roots* at the level of C5-C7, grey and white matter were manually segmented. Ventral and dorsal nerve roots were reconstructed based on qualitative assessment using 'SEED', 'AND', and 'NOT' ROIs to select and remove fiber tracts belonging or not corresponding with the known anatomy. Values for the FA, mean diffusivity (MD), AD, and RD of the grey and white matter (C5-C7), and of each cervical spinal cord were computed.

2.5. The cervical peripheral nerves (C4-C8)

The *cervical peripheral nerves* (C4-C8) were reconstructed using a tract based analysis as described by [15]. In short 'SEED', 'AND', and 'NOT' ROIs were used to reconstruct fiber tracts. At each level where the nerve branched with the spine, a segment of 3 cm was selected. Based on these segmentations, values for the FA, MD, AD, and RD of the cervical nerves (C4-C8) were computed.

2.6. Histological examination

Tissue samples of the spinal cord and peripheral nerve roots at the level of C5-C7 were obtained during the autopsy one day after the MRI examination. The tissue samples were marked at the position of C5 to indicate cranial-caudal and were then preserved in formaldehyde. Klüver Barrera staining was used for the histological section preparation [21]. Ten histological sections per tissue sample were compared with the anatomical MRI and the "high in-plane" DTI protocol at all levels (10 per subject).

3. Results

3.1. Data acquisition

Image quality of all DTI datasets was sufficient for analysis. The anatomical MRI data was suitable for analysis in 40 out of 50 slices (five slices of subject 4, and five slices of subject 5 were not sufficient due to a low image quality). Example data of the "high in-plane" and "isotropic" DTI protocol before and after correction is shown in Fig. 1. The effect of data correction is best observed in the color-encoded FA, and the grayscale maps. While it is difficult to indicate the corrections in the raw date (Fig. 1 first and second row), the difference in uncorrected and corrected data in the FA and MD maps were apparent (Fig. 1 third, fourth and fifth row). The color-encoded FA map of the "high in-plane" protocol shows that the grey and white matter boundary is more accurately defined and that eddy current induced artifacts are reduced after image correction. The latter is best seen at the edges of the spinal