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# Clinical Study

# Diffusion tensor imaging for anatomical localization of cranial nerves and cranial nerve nuclei in pontine lesions: Initial experiences with 3T-MRI



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#### ABSTRACT

With continuous refinement of neurosurgical techniques and higher resolution in neuroimaging, the management of pontine lesions is constantly improving. Among pontine structures with vital functions that are at risk of being damaged by surgical manipulation, cranial nerves (CN) and cranial nerve nuclei (CNN) such as CN V, VI, and VII are critical. Pre-operative localization of the intrapontine course of CN and CNN should be beneficial for surgical outcomes. Our objective was to accurately localize CN and CNN in patients with intra-axial lesions in the pons using diffusion tensor imaging (DTI) and estimate its input in surgical planning for avoiding unintended loss of their function during surgery. DTI of the pons obtained pre-operatively on a 3 Tesla MR scanner was analyzed prospectively for the accurate localization of CN and CNN V, VI and VII in seven patients with intra-axial lesions in the pons. Anatomical sections in the pons were used to estimate abnormalities on color-coded fractional anisotropy maps. Imaging abnormalities were correlated with CN symptoms before and after surgery. The course of CN and the area of CNN were identified using DTI pre- and post-operatively. Clinical associations between post-operative improvements and the corresponding CN area of the pons were demonstrated. Our results suggest that pre- and post-operative DTI allows identification of key anatomical structures in the pons and enables estimation of their involvement by pathology. It may predict clinical outcome and help us to better understand the involvement of the intrinsic anatomy by pathological processes.

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### 1. Introduction

Due to the complex and dense anatomy of the brainstem, surgery on and visualization of pontine lesions in relation to cranial nerves (CN) and cranial nerve nuclei (CNN) remain challenging for neurosurgeons and neuroradiologists. With continuous development of surgical techniques and neuroimaging, the management of those lesions is improving. MRI techniques, in particular diffusion tensor imaging (DTI), have been proven to provide reliable anatomical–structural information in various areas of the brain [1–5]. The region of the pons, which represents an exceptional visualization challenge due to its densely packed anatomical structures, has been the focus of several investigations using DTI [3,6–8].

The brainstem encompasses areas with highly eloquent functions that are under constant risk of damage by surgical manipula-

tion. Among them, certain CN and CNN play a critical role in normal functioning. Their pre-operative localization in the presence of pathology is challenging, but nevertheless can contribute to avoiding unintended loss of function and undoubtedly creates an advantage for surgical outcomes.

Although DTI provides valuable information about the distortion and interruption of corticospinal and sensory tracts in the infratentorial area, the exact anatomical localization of CN and CNN in relation to brainstem lesions has not yet been systematically studied to our knowledge. According to current literature [9] and anatomical textbooks [10] CN and CNN are symmetrically located around and within the pons.

In recent years we have been using DTI routinely for pre- and post-operative visualization and surgical planning in patients harboring lesions in the infratentorial area of the brainstem. We present our experience using DTI to visualize certain CN and CNN in seven patients with brainstem cavernomas (BSC) in regard to pre-operative planning and post-operative clinical outcome.

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Our goal was to determine whether it is possible to identify CN and CNN for surgical guidance and improved clinical outcomes with current DTI technology.

#### 2. Patients and methods

#### 2.1. Patient characteristics

This retrospective single-center study included seven patients (six women, one man) with a mean age of 36 years (standard deviation 15 years; range 19 to 50 years, Table 1). Each underwent microsurgical resection of a symptomatic BSC. All procedures and imaging were performed in accordance with the routine institutional guidelines after receiving the patient's written consent. All BSC were located in the pons (Table 1).

## 2.2. Clinical assessment and cranial nerve deficits

Patient data, including CN deficits, were retrospectively obtained upon admission and once again on discharge with a special focus on CN V–VII. The neurological status of all patients during the pre-operative period and upon discharge was classified with a modified Patzold Rating [11,12]. This rating tests CN, motility, motor disturbances, pathological reflexes, sensory deficit, gait disturbances, and psychological symptoms to achieve a grading of functional disturbances. Patzold Rating scores represent a weighted sum of clinical symptoms. The rating was assessed 1 day before surgery and 1 day after surgery. All clinical information was retrospectively derived from official admission reports, clinical notes and discharge letters. Histopathological analysis of the resected lesions revealed cavernoma malformations in all seven patients.

# 2.3. Conventional MRI data acquisition and DTI data post-processing

All radiological images were provided and analyzed by the Department of Neuroradiology, University of Zurich. T1- and T2-weighted MRI, as well as DTI studies, were obtained as part of the pre- and post-operative routine at this institution. A 3 Tesla (3T) whole body MRI system (Philips Achieva, Best, Netherlands), equipped with 80 mT/m/ms gradient coils and an eight element receive head coil array (MRI Devices, Waukesha, WI, USA), was used for imaging studies in patients with BSC. Each imaging session included DTI and an anatomical imaging study, including a gadolinium enhanced scan for intra-operative navigation. The field of view for all scans was defined as  $200 \times 200 \text{ mm}^2$ . For the DTI series, a whole brain diffusion-weighted single-shot spin-echo echo planar imaging sequence was applied with the following parameters: in-plane matrix =  $96 \times 96 \text{ mm}$ , reconstructed to

**Table 1**Clinical and surgical characteristics of patients

Patient Volume (mm<sup>3</sup>) Cranial nerve deficits Patzold Age Sex Location Approach 0 0 1 0 CN VI CN VI CN VII CN VII CN V CN V 1 47 F Pons 21.1 Suboccipital Υ Υ 17 17 2 39 F 174 Retromastoidal γ Υ Ν Ν Ν Ν 7 6 Pons N Y Y 3 32 F Pons 15.7 Temperobasal Υ Υ N 18 6 44 F 21 Pons 14.9 Suboccipital N N Ν 50 Y Y N 23 5 M Pons 9.2 Suboccipital N N 19 6 22 F 3.8 Ν Y Y Ν 13 9 Pons Suboccipital Ν Ν F 19 Retromastoidal Ν Ν 10 7 Pons 0.6 8 7 Minimum 19 0.6 6 39 17 Median 6 1 8 28.9 23 19

 $128 \times 128$  mm, 60 contiguous slices, slice thickness = 2.1 mm, echo time = 50 ms, number of signal averages = 2, and 60% partial k-space acquisition. Diffusion weighting with a maximal b-factor of  $1000 \text{ s/mm}^2$  was carried out along 15 icosahedral directions complemented by one scan with b = 0. The DTI time was approximately 5 minutes.

Axial, coronal and sagittal images of the color-coded fractional anisotropy (FA) maps were analyzed for identification of consistent anatomy and structures of CN and CNN V, VI and VII. A standard color scheme was used in the Philips software to encode the FA maps, with blue indicating superior to inferior direction, red indicating transverse direction and green indicating anterior-posterior direction. Anatomical key locations of CN and CNN V, VI and VII and white matter tracts were identified by comparing MRI and color-coded FA maps. Figure 1 illustrates the estimated location and extent of CNN, CN and major tracts that are critical in the lower pons. Images were subsequently compared with anatomical sections of the pons from an anatomical brainstem atlas [10].

#### 2.4. Surgical procedure

All patients underwent microsurgical resection of the symptomatic BSC in the pons. Surgical approaches depended on the size and location of the lesion and included four suboccipital, two retromastoid and one temporobasal approaches. Multimodal intra-operative monitoring was used to support the surgeon and included motor evoked potentials [13], somatosensory evoked potentials [14], acoustic evoked potentials, neuronavigation and mapping of the rhomboid fossa [15]

#### 3. Results

#### 3.1. Illustrative patients

## 3.1.1. Illustrative Patient 1

Supplementary Figure 1A illustrates the typical case of Patient 6. This 22-year-old woman had a BSC malformation (3.8 mm³) in the right central part of the pons. On admission she presented with hemiparesis and CN deficit VI and VII. CN V was intact. On axial FA color-coded maps CN V showed up as sagittal fibers in green. The major FA map findings were distortion in the area of CN VI and VII. This correlated well with the space occupying effect of the lesion and the CN deficits of the patient. Furthermore, the intact cisternal course of CN V was displayed. This was reflected by the absence of relevant clinical symptoms. The transverse pontocerebellar fibers formed red bands as they cross the pons, but turned green (indicating sagittal direction) as they curved dorsally and merged into the sagittal fibers of the middle cerebellar peduncles. The corticospinal tracts formed blue bundles as they descended

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