## Diffusion tensor MRI and tractography of the sacral plexus in children with spina bifida

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**Background and purpose**: Patients with spina bifida (SB) generally suffer from neurogenic bladder dysfunction and affected sensory and motor innervation of the lower limbs [1]. It is still largely unknown how neural tube defects in spina bifida (SB) affect the nerves at the level of the sacral plexus. Information regarding the 3D anatomy and tissue properties of the sacral plexus can be helpful to better understand the mechanism of disturbed innervations of the bladder in children with SB. It potentially can alter treatments plans to enhance lower urinary tract innervation by rerouting nerves. Therefore the aim of this study was to reconstruct and visualize the sacral plexus in SB patients and to investigate nerve tissue properties with diffusion tensor imaging (DTI) and fiber tractography (FT) in addition to conventional MRI.

**Methods**: Local institutional review board approval was obtained for this study and written informed consent was given prior to the MRI examination. 10 SB patients (8-17 years) underwent DTI on a 3 Tesla MR system (Achieva; Philips Healthcare, Best, The Netherlands) using a 16-channel phased-array surface coil. DTI was performed with diffusion-weighted spin echo single-shot echo planar imaging (EPI) in the axial plane with the following parameters; TE = 44 ms, TR = 9683 ms, SENSE factor 2, number of excitations = 2, FOV 288 × 204 mm², matrix size  $96 \times 68$ , 55 slices with thickness = 3.0 mm, resulting in a voxel size of  $3.0 \times 3.0 \times 3.0$  mm³, SENSE factor 2, half scan 0.6, EPI train length (ETL): 25, SPAIR fat suppression, b-values 0 en 800 s/mm², and 15 gradient directions. The total acquisition time was 11:46 minutes. In addition, a 3D Turbo Spin Echo (3D-TSE) scan was acquired with parameters: TR = 3000 ms, TE = 286, TSE factor 180, startup echoes 4, FOV  $250 \times 250 \times 100$  mm², matrix size  $250 \times 250 \times 100$ , reconstruction matrix  $512 \times 512 \times 200$ , resulting in a voxel size of  $0.49 \times 0.49 \times 0.5$  mm³, number of excitations 2, SENSE factor 2, SPAIR fat suppression and total acquisition time of 10:03 minutes as described by van der Jagt et al [2]. FT was performed with the diffusion MRI-toolbox *ExploreDTI* to determine tract based fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) in the sacral plexus of SB patients. Results were compared to 10 healthy controls as obtained in the study by van der Jagt et al [2] with the non-parametric Mann-Whitney U test.

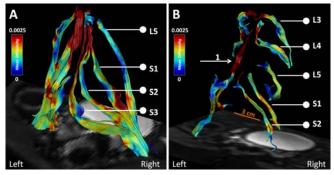


Figure 1: Lower lumbar and sacral nerves, A) healthy control, B) spina bifida patient with myelomeningocele at the level of L4/L5/S1. L5 on the left side is not visible (indicated with 1), the sacral nerves do not connect with the spinal cord.

A trajectory originating from S2-S4 and continuing to the bladder was found in three patients (see figure 2A for an example in one patient). Although this could not be confirmed by the anatomical images, it is likely that this is the pudendal nerve, as it shows the same course as presented on a schematic anatomy configuration of the sacral plexus (see figure 2B).

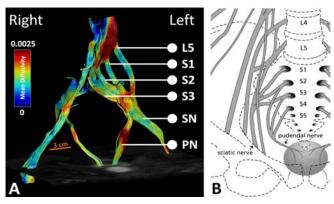


Figure 2: A) Anterior view of a spina bifida patient with myelomeningocele at the level of L1-L4, the pudendal nerve is indicated with "PN", and the sciatic nerve with "SN", B) schematic overview of the lumbosacral nerves. The sacral branches and pudendal nerve in Fig. A correspond with the anatomy shown in Fig. B.

**Results**: This 3-Tesla DTI study was able to reconstruct the 3D architecture of the sacral plexus in 10 SB patients, detailing the individual pathway trajectories and the microstructural properties of L4-S3. Nerves of SB patients showed to a large extent asymmetry and disorganisation compared to healthy controls (see figure 1).

Especially at the level of the myelomeningocele, it was difficult to find a connection with the cauda equina, although this was visible on the anatomical image. In two SB patients, nerves at the level of L5 could not be reconstructed with FT despite the fact that they were visible on anatomical images. Furthermore, the MD, AD, and RD values in S1-S3 were significantly lower in the SB patients (see table 1).

Table 1 Diffusion parameters (MD, AD, and RD) of SB patients and healthy controls

Nerve	Diffusivity (mm <sup>2</sup> /s) x 10 <sup>-3</sup>					
•	MD		AD		RD	
	Healthy	SB	Healthy	SB	Healthy	SB
L4	1.34±0.22	1.32±0.16	1.72±0.22	1.70±0.18	1.15±0.21	1.14±0.15
L5	$1.42\pm0.21$	1.31±0.24	1.86±0.24	1.72±0.31	1.19±0.20	1.11±0.21
S1 <sup>a</sup>	1.83±0.24	1.40±0.22	2.31±0.27	1.78±0.23	1.59±0.22	1.22±0.23
S2a	1.73±0.29	1.36±0.21	2.13±0.36	$1.70 \pm 0.21$	1.530.26	1.19±0.22
S3 <sup>a</sup>	1.62±0.32	1.33±0.23	1.98±0.39	1.66±0.35	1.43±0.29	1.17±0.22
<sup>a</sup> S1, S2, and S3: MD, AD, and RD significantly different: p<0.01						

Conclusion: This 3T MRI study shows for the first time asymmetry and disorganization of the sacral plexus in 10 SB patients with DTI and FT. Due to the complex disorders and broad anatomical variations in SB patients, it is the difficult interpreting the DTI and FT based results in an unambiguous way. However, the observed difference in diffusion values show that these methods can be used to identify nerve abnormalities. In conclusion, DTI and diffusion values show abnormalities in comparison to healthy controls. Combining anatomy, DTI, and diffusion values and correlating them to the neurological problems of SB patients, can provide a valuable contribution to a better analysis and understanding of neurological problems of these patients in the future.

## References:

- 1. Özek MM, Cinalli G, Maixner WJ. Spina bifida management and outcome. New York: Springer; 2008.
- 2. van der Jagt PKN, Dik P, Froeling M, et al. Architectural configuration and microstructural properties of the sacral plexus: A diffusion tensor MRI and fiber tractography study. NeuroImage. 2012;62(3):1792-9.