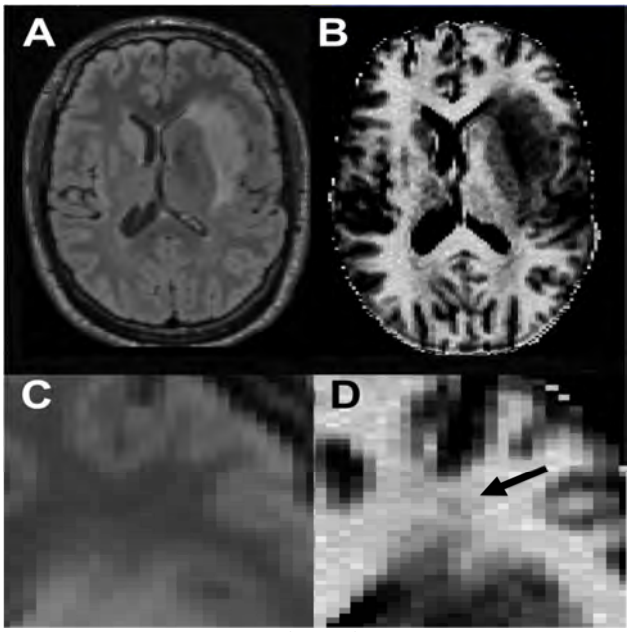
# Peritumoral Myelin Imaging In Low-Grade Astrocytomas

Hagen H Kitzler[1], Hannes Wahl[1], Tareq Yuratli[2], and Matthias Meinhardt[3]

*[1]Neuroradiology, Technische Universitaet Dresden, Dresden, SN, Germany, [2]Neurosurgery, Technische Universitaet Dresden, Dresden, SN, Germany, [3]Neuropathology, Technische Universitaet Dresden, Dresden, SN, Germany*

**Introduction:** Astrocytomas are infiltrative tumors derived from central nervous system glia cells. They arise in white matter (WM) and use its intrinsic structures to infiltrate adjacent and remote tissue areas. Little is known about the peritumoral WM changes although specific tissue destruction mechanisms altering the peritumoral tissue composition may precede the infiltrative process[1]. We used the whole-brain relaxation method *Multi-component Driven Equilibrium Single Pulse Observation of T1 and T2* (mcDESPOT) that allows the evaluation of myelination by means of measuring the myelin volume fraction (VFM)[2]. Its capability to retrieve isotropically resolved whole brain VFM maps enables to retrieve myelination information in tumors and the adjacent peritumoral tissue. We hereby present a new approach to quantify specific peritumoral tissue demyelination to study its relationship to focal tumor progress/infiltration over time and the feasibility to correlate relative magnetic resonance imaging measures of myelination with histological quantification of myelin alteration.

**Methods:** A 1.5T MR scanner (Siemens Sonata, Siemens AG, Erlangen Germany) and 8-channel head RF coil were used to derive multi-component T1 and T2 information from sets of *Fast Low Angle SHot* (FLASH) and true *fast imaging with steady state precession* (TrueFISP) data acquired over a range of flip angles at constant TR with FOV=22cm, matrix=128x128, slice thickness= 1.7mm; FLASH: TE/TR=2.0/5.7ms, $\alpha$={5,6,7,8,9,11,13,18}°; TrueFISP: TE/TR=1.71/3.42ms and $\alpha$={9,14,19,24,28,34,41,51,60}°. The total mcDESPOT imaging time was ~13min. VFM maps were derived using the established mcDESPOT processing method[2]. An additional 3D-fluid attenuated inversion recovery (FLAIR) sequence was obtained to segment the tumors and the adjacent WM as volumes of interest. Three patients with low-grade actrocytomas WHO II (world health organization grading) were recruited before operative therapy. Intraoperatively retrieved tissue specimen were dyed for myelin sheaths and HE and analyzed in correlation to its location (1) within the tumor, and (2) at the adjacent tumor WM tissue. Imaging data post processing involved brain extraction and co-registration to compare the conventional FLAIR and quantitative myelin imaging pattern of the tumors[3].



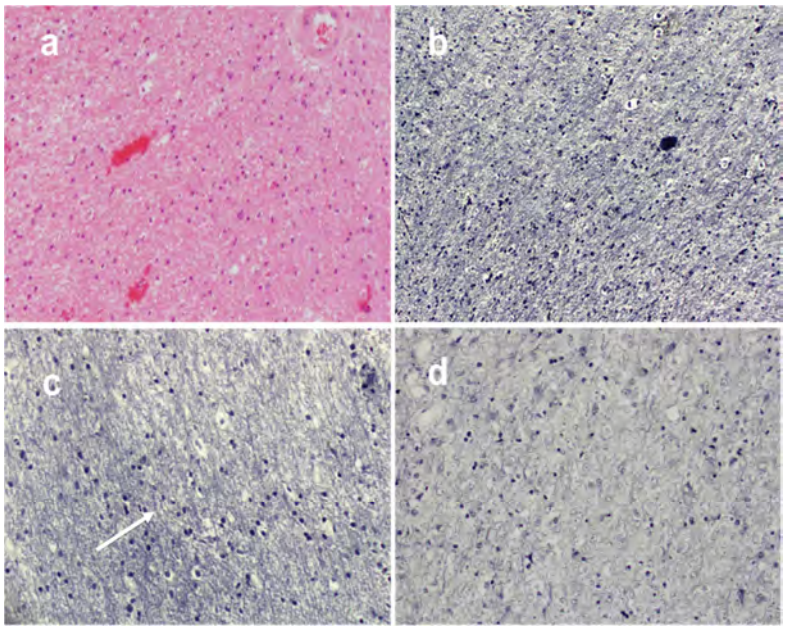




***Fig.1*** MRI: FLAIR images of an infiltrative astrocytoma in deep WM approaching the frontal WM (A) with a zoomed section showing a well-defined tumor margin (C). The VFM demonstrates marked myelin loss in the central tumor core (B) and the zoomed section reveals measurable myelin reduction even exceeding the tumor margin.

***Fig.2*** Histology: HE stain of tumor adjacent WM with single tumor cells but preserved myelin and oligodendrocyte density (a). Myelin silver stain in healthy WM shows normal density of myelin sheaths and oligodendrocyte nuclei (b), which are almost entirely eliminated in the tumor core (d). The tumor adjacent WM shows a demarcation line (*arrow*) between normal WM and marked myelin and oligodendrocyte loss with only scattered tumor cells and no edema.

**Results:** The specific analysis of mcDESPOT derived whole-brain VFM maps allowed the assessment of individual WM myelination within tumors and the surrounding tissue. Imaging data showed marked reduction of VFM within the tumor cores in correlation with histologically probable loss myelin sheaths. However, the tumor adjacent WM revealed notable but inhomogeneous reduction of VFM. Histology unfolded areas of (1) oligodendrocyte reduction (myelin maintanance), and (2) reduction of myelin sheath density. The mcDESPOT derived measure mean VFM was found 0.014 ± 0.034 in central tumor cores and 0.221 ± 0.018 tumor adjacent WM.

**Discussion/Conclusion:** Astrocytic tumor invasion is not fully understood yet and imaging research focuses on the tumor tissue itself. This feasibility study demonstrates subtle peritumoral myelin loss measurable with myelin imaging using the mcDESPOT acquisition. Prospective application may reveal the relationship of peritumoral WM decay and tumor invasion. An *in vivo* predictor may be of great clinical value, since infiltration and mass effects are limiting factors of therapy and survival.

**References:** [1] Hwang et al. Acta Neurochir. 1986;80(3-4):128-30 [2] Deoni et al., Magn Reson Med. 2008; 6: 1372-87

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