

## MR FOLLOW-UP OF GLIOBLASTOMA PATIENTS TREATED WITH DENDRITIC CELL IMMUNOTHERAPY: THE ROLE OF DWI AND PWI.

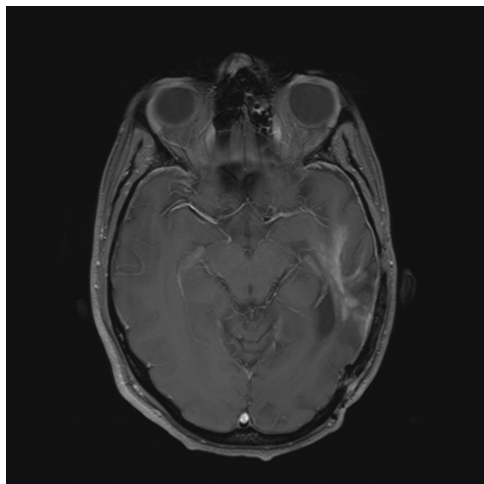
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**Introduction:** Malignant gliomas (WHO grade III and IV gliomas) are the most common and aggressive brain tumours. Dendritic cell (DC) immunotherapy is a novel treatment for high-grade gliomas, that appears a promising and feasible treatment for inducing long term survival in at least a subpopulation of these patients. In the imaging follow-up of DC immunotherapy patients, the vaccine-induced inflammatory immune response commonly presents as contrast enhancement in the brain parenchyma on MR imaging. The contrast enhancement can be quite remarkable and the differentiation between the inflammatory response, when presenting with contrast enhancement, and early tumour relapse can be challenging, as the conventional MR imaging characteristics of both entities are similar (Figure 1).

Our study evaluates the potential use of magnetic resonance (MR) diffusion weighted imaging (DWI) and MR perfusion weighted imaging (PWI) as markers for distinguishing dendritic cell immunotherapy post vaccination inflammatory response from recurrent glioblastoma tumour growth.

**Methods:** Patients with relapsed glioblastoma, who could obtain a total or near-total resection and be rapidly weaned from corticosteroids within 1 to 2 weeks after surgery were included in the HGG-2003- immunotrial. A retrospective analysis of 32 follow-up MRI examinations (mean follow-up time 21 months) with DWI and PWI in 8 patients who underwent post-operative DC immunotherapy was performed for this study. The 32 total examinations, performed in 8 patients at 2 to 8 different time points per patient were grouped into three groups.



**Figure 1** A patient who underwent postoperative DC immunotherapy presented with a contrast-enhancing lesion at regular MR follow-up. At this time point it was not possible to make the differentiation of tumor progression vs. treatment induced changes from the conventional imaging sequences.

All examinations performed in patients that remained clinically and radiologically stable during the follow-up (mean follow-up period 20.5 months) were grouped into group 0 – stable. Examinations performed in patients that had tumour progression during the follow-up period (mean follow-up period 21.5 months) were divided into group 1a – examinations that had been performed at time points before distinct progression and group 1b – examinations performed after progression.

To define distinct clinical or radiological progression, we adopted the criteria currently used in the clinical setting in the follow-up of recurrent GBM patients: a significant increase in contrast enhancement in or surrounding the resection area in more than two consecutive imaging time points on T1-weighted post-contrast images or a severe progressive clinical neurological deterioration. Mean and minimum ADC values of the enhancing lesion and maximum rCBV ratios of the lesion were measured.

**Results:** Maximum rCBV ratios were significantly higher in group 1a ( $4.87 \pm 1.61$ ), compared to stable patients ( $1.22 \pm 0.47$ ,  $p < 0.001$ ). Maximum rCBV ratios were significantly higher in group 1b ( $9.25 \pm 2.68$ ), both compared to values measured in stable patients ( $p < 0.001$ ) as well as group 1a ( $p = 0.017$ ). The mean ADCs in the contrast-enhancing region were  $1.53 \pm 0.42$ ,  $1.28 \pm 0.17$  and  $1.20 \pm 0.17 \times 10^{-3} \text{ mm}^2/\text{s}$  in groups 0, 1a and 1b, respectively. There was a trend for the ADC values to be lower in group 1a than group 0 and lower in group 1b than 1a, but the difference was not significant ( $p = 0.11$ ,  $p = 0.43$ ). The difference between groups 0 and 1b was also insignificant ( $p = 0.08$ ). Minimum ADCs in the contrast-enhancing regions were lower in group 1a ( $0.62 \pm 0.06 \times 10^{-3} \text{ mm}^2/\text{s}$ ) than in group 0, ( $1.03 \pm 0.43 \times 10^{-3} \text{ mm}^2/\text{s}$ ,  $p = 0.01$ ) and higher in group 1b ( $0.76 \pm 0.08 \times 10^{-3} \text{ mm}^2/\text{s}$ ) compared to 1a ( $p = 0.02$ ).

**Conclusion:** Our preliminary findings suggest that maximum lesional rCBV and minimum ADC values in the contrast enhancing lesions may be used to help distinguish between dendritic cell immunotherapy post vaccination inflammatory response and recurrent glioblastoma tumour growth in patients with recurrent glioblastoma, treated with dendritic cell immunotherapy.