

Prognostic factors in astrocytoma WHO II after radiotherapy – role of MRI follow-up in therapy outcome

C. Plathow¹, M. P. Lichy², D. Schulz-Ertner³, I. Zuna², P. Bachert², J. Debus¹

¹German Cancer Research Center/ University of Heidelberg, Heidelberg, BW, Germany, ²German Cancer Research Center, Heidelberg, BW, Germany, ³University of Heidelberg, Heidelberg, BW, Germany

Synopsis

MRI follow-up was performed in 139 patients with astrocytoma WHO II after fractionated stereotactic radiotherapy (FSRT).

Pre-therapeutic contrast-enhancement (CM-enhancement) in the MRI proved to be a significant predictor for progression-free survival (PFS) and overall-survival (OS).

Pre-therapeutic CM-enhancement must be interpreted as a sign of higher-malignisation. MRI provides the opportunity to identify regions of higher-malignisation prior to radiation therapy treatment planning. This offers the possibility to adapt therapy (RT+/- CHT). Whether additional diagnostic examinations like FDG-PET and MRI spectroscopy contribute to the diagnostic specificity remains to be shown.

Introduction

Radiotherapy is a frequent procedure in the management of astrocytoma WHO II^{1,2,3}, a tumor with a high tendency to recur even after RT (~90% of the recurrences are located in the former high-dose area)^{4,5}. FSRT is a technique which irradiates the target volume with high precision and at the same time reduces doses within healthy tissue. The diagnostic follow-up, especially by MRI, is essential for an accurate RT-treatment planning. Pre-therapeutic CM-enhancement is controversially discussed as a potential predictor for outcome^{6,7}. We investigated patients with and without pre-therapeutic CM-enhancement in the MRI and the influence on PFS and OS.

Material and Methods

139 patients with histologically proven astrocytoma WHO II have been treated with FSRT at our institution. Median age was 40.5 years (61.8% male, 38.2% female). 72 patients were CM+ and 67 patients CM- prior to FSRT. All patients had 3D treatment planning, the planning volume was defined as signal abnormality on T2w MRI plus a safety margin of 1cm. All patients had for follow-up radiographic studies with MRI 1.5 T (Magnetom Vision[®]; Magnetom Symphonie[®]; Siemens; Germany) 6 weeks after completion of RT and in 3 months intervals, thereafter. MR imaging included multiplanar Gd-DTPA enhanced T₁ and T₂ sequences for radiation planning and follow-up (SE T₁w (512 matrix 4-5mm planar slice thickness), SE T₁w (512 matrix 3-5mm coronal slice thickness), TSE T₂w and FLAIR (512 matrix 5mm planar slice thickness)). Tumor response was scored according to the following criteria: complete response (CR); partial response or regression (PR, >50% reduction in T₂); no change (NC, not qualifying for complete or partial response); progression (P, >25% increase in tumor size¹). In this study a focus was set on MRI follow-up for the investigation of signs of a tumor progression. PFS and OS rates were calculated using the Kaplan Meier method. Univariate analysis was performed.

Results

Median follow-up was 44 months. Actuarial PFS was 39% at 5 years, OS was 58%. Median progression-free survival was 37 months. 91.3% of all relapses occurred within the former high-dose area. CM-enhancement prior to FSRT proved to be a significant prognosticator for PFS (2 years vs. 4.8 years, p<0.0001, Fig. 1) and OS (5 years vs. 8.75years, p<0.01, Fig. 2). CM+-patients showed from the 1st year after FSRT significant higher rates of a recurrence (p<0.001, Fig. 3), whereas CM--patients had a steady progression after about 3 years in the MRI. 6.9 years after FSRT, all CM+-patients showed radiographic signs of a recurrence in the MRI. Fig. 3 shows the frequency of tumor progression in the MRI in comparison to treated patients of the group within time.

Conclusion

MRI follow-up in astrocytoma WHO II is a feasible technique and allows differentiation between patients with different clinical outcome. Pre-therapeutic CM+-patients have a significant worse PFS and OS compared to CM--patients. CM enhancement must therefore be interpreted as a sign of higher-malignisation. MRI is able to identify regions of potential higher-malignisation pre-therapeutically. This offers the possibility to adapt therapy (RT+/- CHT) e.g. target doses might be escalated within these regions. So frequent MRI-follow is useful in CM+-patients even though further therapy regimen often are limited by the high aggressivity of the tumor and frequent higher primary RT-doses compared to CM--patients. CM--patients have steady signs of progression especially 3 years after FSRT. In this group a frequent MRI follow-up is essential as salvage therapy with reirradiation using stereotactic RT-techniques or second line chemotherapy has proven to prolong survival². Often conventional MRI is the first hint for tumor

progression. Verification by other techniques can be indicated. Whether additional diagnostic examinations like FDG-PET or ¹H spectroscopic imaging contribute to the diagnostic specificity remains to be shown⁸.

Figure 1: Kaplan-Meier of progression-free survival

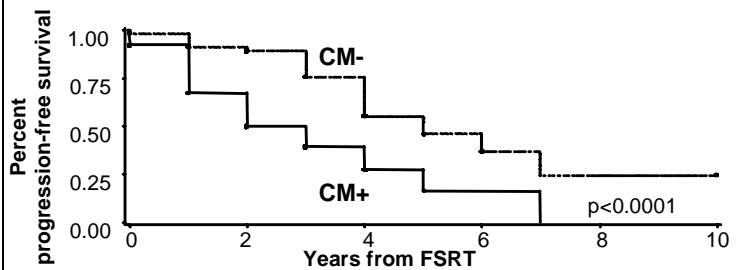


Figure 2: Kaplan-Meier of overall survival

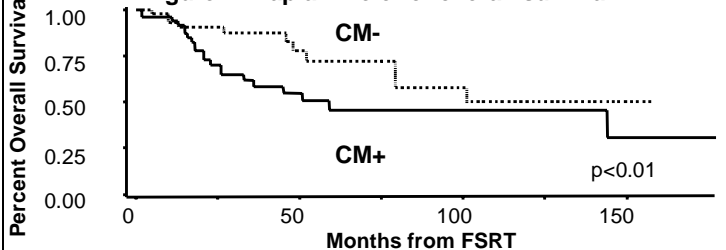
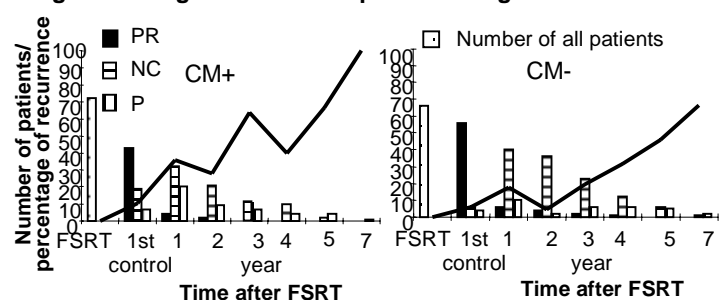


Figure 3: Diagnostic follow-up - Percentage of recurrence



¹ Shaw E, et al. JCO 20: 2267 – 2276, 2002.

² Herfarth KK, et al. Semin in Surg Oncology 20: 13-23, 2001.

³ Leighton C, et al. JCO 15: 1294 – 1301, 1997.

⁴ Plathow C, et al. International Journal of Radiology and Biological Physics 51: 203 – 204, 2001 (abstr).

⁵ Van Kampen M, et al. Radiology 201: 275 – 278, 1996.

⁶ Kreth FW, et al. Cancer 79: 370-379, 1997.

⁷ Philippon JH, et al. Neurosurgery 32: 554-559, 1993

⁸ Lichy MP, et al. In: "Proceedings, 10th Annual Meeting, ISMRM, Honolulu" 2002; 1: 575.