

The Importance of Extent of Resection on Overall Survival in Primary Glioblastoma – Follow Up Results of a Randomized Trial

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Introduction

In a randomized controlled trial (RCT) the use of an intraoperative MRI (iMRI) led to improved rates of complete tumor removal [1]. In this study, gross total removal (GTR) was associated with longer progression-free survival. However, overall survival (OS) was not addressed in the primary analysis.

Methods

We performed a secondary analysis of survival data of patients with histologically proven and previously untreated glioblastomas (GBM) who had participated in a RCT comparing conventional with iMRI guided microsurgery. Preoperative and early postoperative MRI scans were assessed for extent of resection (EOR) by an independent and blinded radiologist and classified accordingly:

- complete removal of enhancing tissue, CRET
- gross total removal, GTR (residual enhancing tissue, not exceeding 0.175ccm)
- subtotal removal, STR (residual enhancing tissue, exceeding 0.175ccm)

Adjuvant therapy was administered according to interdisciplinary board decision and patient preference. The trial was registered with clinicaltrials.gov, number NCT01394692.

Results

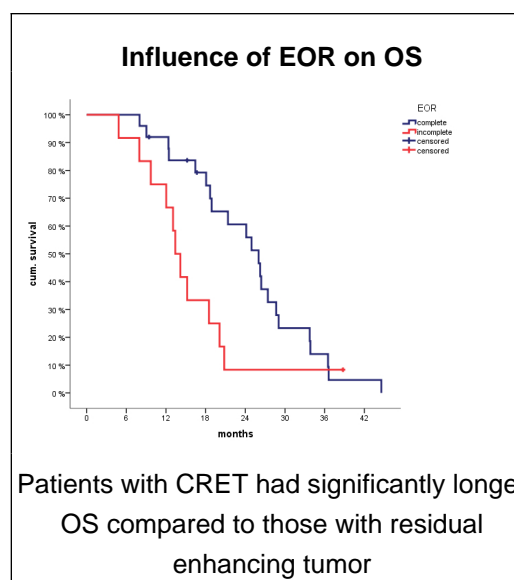
We analyzed imaging and survival data of 37 patients with a median age of 56 years (range: 30-76). No patient was lost to follow-up. Median OS was 18.9 months (95% -confidence interval: 15.9-21.9).

While the use of iMRI itself did not affect outcome ($p=0.44$), patients undergoing iMRI-guided resection had a higher rate of GTR as well as CRET than those undergoing conventional microsurgery ($p<0.05$ and $p<0.01$, respectively).

Influence of iMRI use on EOR			
	CRET (n)	GTR/STR (n)	total (n)
iMRI group	17	2	19
conventional group	8	10	18
total	25	12	37

	CRET/GTR (n)	STR (n)	Total (n)
iMRI group	18	1	19
conventional group	12	6	18
total	30	7	37

Significantly higher rates of CRET ($p<0.01$) and GTR ($p<0.05$) were achieved using iMRI compared with conventional microsurgery



CRET was associated with improved OS (median 24.9 vs. 13.4 months, $p<0.05$). There was a trend for clinical status influencing OS: patients with KPS ≥ 90 had an OS of 24.1 months, while it was only 13.4 for patients with KPS ≤ 80 ($p=0.06$).

MGMT promotor methylation status did not affect OS on a statistically significant level ($p=0.33$). Likewise, patient age was not a statistically significant factor concerning OS ($p=0.48$). Following Cox regression analysis, CRET in contrast to KPS remained the only statistically significant factor influencing OS ($p<0.05$).

Conclusions

Our data, derived from an RCT, corroborate the findings of a recently published paper that showed superiority of gross total vs. subtotal resection of GBM in regards to OS [2].

We could show that using an iMRI helps to achieve a greater extent of resection and thus directly impacts patient outcome.

Learning Objectives

- CRET is one of the most important prognostic factors for patients with GBM
- iMRI helps to maximize extent of resection

References

- 1.Senft C, Bink A, Franz K, Vatter H, Gasser T, Seifert V. Intraoperative MRI guidance and extent of resection in glioma surgery: a randomised, controlled trial. *Lancet Oncol.* 2011; 12(11): 997-1003.
- 2.Kreth FW, Thon N, Simon M, Westphal M, Schackert G, Nikkhah G, Hentschel B, Reifenberger G, Pietsch T, Weller M, Tonn JC, German Glioma Network. Gross total but not incomplete resection of glioblastoma prolongs survival in the era of radiochemotherapy. *Ann Oncol.* 2013; 24(12): 3117-3123.