



Evaluation of surgical decision making and resulting outcome in patients with highly eloquent glioblastoma: Results of a multicenter assessment



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ABSTRACT

Introduction: Treatment of glioblastoma (GB) patients amenable only for a subtotal resection (STR) is controversial. Since outcome of patients is affected by surgical management, our aim was to assess surgical decision making and resulting outcome in patients with highly eloquent GBs.

Patients and methods: We retrospectively assessed GB patients with intended sub-total resection (STR) or stereotactic biopsy (STX) of 3 neurooncological centers operated between 2008 and 2013. A volumetric assessment of overall extent of resection (oEoR), presence of complications, new permanent neurological deficits (nPNDs) was performed. A central reviewer reassessed all cases blinded and gave recommendation on surgical management and on a potential EoR (pEoR) based on imaging data. We compared outcome data using Mann-Whitney-U-test and Sign-Rank-Test. Survival was assessed based on Kaplan-Meier-estimates.

Results: 97 patients were included. In 17 patients received STX, 70 patients a STR and 10 patients a near total resection (NTR, EoR > 95%). Median OS was significantly different from STX patients only if NTR was reached (16 vs. 7 months, $p = 0.042$). The central reviewer recommended a more aggressive strategy (NTR or STR resp.) in 41 patients and a less aggressive strategy in 13 patients. Overall, management recommendation was significantly different to clinical treatment ($p < 0.001$). Mean pEoR was significantly higher than oEoR (85.7% vs. 71.3%, $p = 0.001$). Regarding the different OR subgroups, no significant differences were found in the NTR group (12/13 ties, $p = 1$) and in STX group (14/17 ties, $p = 0.125$). In STR group, a significant difference was found ($p = 0.001$). In 38/69 patients a NTR and in 13/77 patients a STX was recommended.

Conclusion: Surgery in GB patients with intended STR requires precise preoperative planning since potential EoR is mainly underestimated. Especially, patients with lesions amenable for a NTR should not be missed.

1. Introduction

Surgery in patients harboring a glioblastoma remains the primary treatment option; either as microsurgical resection or stereotactic/navigated biopsy (STX) [1]. There are several large series advocating a direct relation of extent or resection and overall survival [2–4]. Yet, in patients not amenable for a gross total resection a controversy exists whether patients do benefit from a STR compared to STX concerning surgical outcome and survival [5] or not [6,7]. Hence, especially in highly eloquent glioblastoma surgical decision making is very challenging. If cytoreductive treatment in these patients is intended current data recommend a minimum resection of 70–78% [8,9]. Thus, neurosurgeons play a crucial role in determining patients' outcome. Therefore, we aimed to assess surgical decision-making in a typical clinical

series of highly eloquent GB in whom only a STR was intended.

2. Patients and methods

2.1. Study design

As part of a multi-center assessment (Neuro-oncological centers of Mainz, Günzburg/Ulm, Stuttgart), we retrieved all patients harboring a primary GB with intended STR and adjuvant radio-chemotherapy in the years 2008–2013. In the current assessment, these patients were compared with a control group of STX patients who had surgery during the same years in one of the centers (Stuttgart).

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2.2. Ethical approval

Ethical approval was received by the ethical board of Ulm University (No: 316/16)

2.3. Patients selection

101 patients met the inclusion criteria. 17 patients after STX and 84 patients after STR were found. 4 STR-patients had to be excluded due to insufficient preoperative imaging. Hence, 97 patients (17 STX and 80 STR) were included in the current assessment.

2.4. Central reviewer's assessment

Basic clinical data and preoperative imaging data of all 97 patients were pseudonymized and evaluated by a senior neurosurgeon (JS) blinded for the primary clinical treatment decision. He made a primary treatment decision categorized as STX, STR or near total resection (NTR). Then, a volumetric assessment of preoperative tumor volume and the potential residual tumor was performed. Volumetric assessment was done using IPLAN 3.0 (Brainlab, Feldkirchen, Germany). The potential residual tumor was defined as highly eloquent areas which were thought to be spared by the central reviewer. The reviewer used all available imaging data like diffusion tensor imaging (DTI) based fiber tracking or functional MRI. Thus, typical areas to be spared could be corticospinal tract, basal ganglia, precentral sulcus, angulate gyrus, arcuate fascicle etc. Infiltration of optic radiation was not considered highly eloquent. None of the GBs was scheduled for awake craniotomy per se reflecting the policy of the associated centers at that time. The central reviewer did not recommend awake surgery either, but recommended STX when the lesion was infiltrating language areas to a large extent. As an additional step for a more conservative approach, the central reviewer added a safety zone of 5 mm residual tumor around

most likely eloquent areas. Fig. 1A shows a typical image of a preoperative tumor volume and Fig. 1B a potential residual tumor volume.

After this step, the reviewer was revealed the postoperative MRI scans (< 72 h) for a review of residual tumor. Base of volumetric assessment was Gd-DTPA enhanced tumor by absence of new diffusion deficits. Fig. 1C shows a typical postoperative volumetric assessment of residual tumor.

2.5. Assessment of outcome parameters

Overall EoR(oEoR) was calculated based on pre and postoperative tumor volume. The potential EoR(pEoR) was calculated based on preoperative tumor volume and potential residual tumor volume as judged by the reviewer. Overall survival(OS) and progression free survival (PFS) were calculated based on patients follow up data, local tumor board protocols and queries of patient registration offices.

Complication and new permanent neurological deficits (nPNDs) were assessed based on patients records at 3months follow up after surgery.

2.6. Specifications of associated centers

All associated centers were using a central oncological board review for decision making in GB patients. We included only patients with a combined radio-chemotherapy according to the EORTC NCIC protocol [10]. Intraoperative monitoring/mapping (IOM) was available at all centers and neuronavigation was used in all centers routinely during the time of assessment. Intraoperative neuronavigation is used in all centers routinely. Concerning intraoperative imaging, one of the centers (Günzburg) was applying intraoperative MRI. None of the patients was operated with adjunct of 5-aminolevulinic acid fluorescence (5-ALA). First routine follow-up was done after 3 months in all centers.

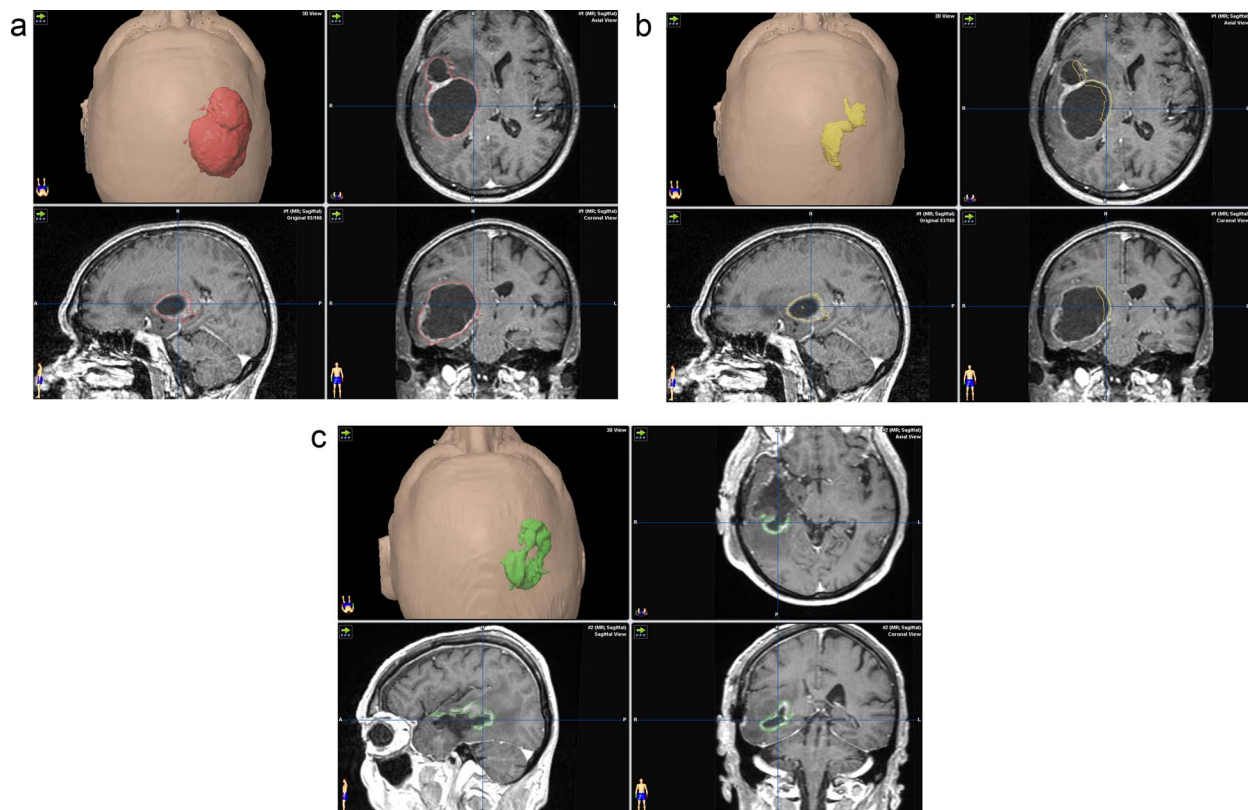


Fig 1. Screenshots of the volumetric assessment using IPLan 3.0 software; (A) preoperative tumor volume; (B) potential residual tumor volume; (C) true postoperative residual tumor volume.

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