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# Maximizing Resection of Diffused Low-Grade Glioma Functional Outcome

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## ABSTRACT

**Background:** most of adults with Diffuse Low Grade Gliomas (DLGGs) are diagnosed with an average age of 39 years and the diagnosis is often made around fully functioning individuals. Currently extent of resection (EOR) is a generally known variable that impacts overall survival (OS), progression free survival and malignant transformation in these gliomas.

**Aim of the study**: this study aimed to evaluate the risks and benefits of maximizing the extent of resection of DLGGS, while preserving neurological function.

**Methodology and Materials:** this was a prospective observational study of group of consecutive 20 patients with initial imaging diagnosis of supratentorial DLGGs. Preoperatively planned for maximal resection even if presuming the proximity of these lesions to eloquent cortex and their relative diffuse nature on imaging. **Results:** 40 % were near eloquent area and 30 % at eloquent areas. GTR achieved in 10% and STR in 65%. Pre-operative Karnofsky Performance Scale (KPS) was 100 in 10%, 90 in 65%, 72 hours post-operative 70 in 60%. During the first 6 months of follow-up KPS was 100 in 60% of the study cohort while only one patient (5%) died. After 6 months KPS was 100 and represented 95% of the whole study. LOS was the longest (4-16 days) in near eloquent and shortest in eloquent (5-8 days). 30% had pre-operative uncontrolled seizures, which cured post-operative, 50% stopped AED within a year. Average back to work period was 2.5 for eloquent, near eloquent 2.8 and non-eloquent 2.6 months.

**Conclusion:** careful pre-surgical planning based on proper reviewed history, recent imaging techniques and utilizing up-to-date intra-operative technology is helping to maximize safe surgical resection, while saving patient function and quality of life.

**Keywords:** astrocytoma, oligiodendroglioma, extent of resection, KPS.

## INTRODUCTION

DLGG normally influence young people who have ordinary life. But, neurological deficits are uncommon in patients with DLGG (Ordinarily diagnosed after seizures); regardless of the possibility that these tumors are located within eloquent areas. This is because of mechanisms of cerebral plasticity, clarified by the way that DLGG is a slowly growing tumor, giving numerous years to the cerebrum for functional remapping with recruitment of perilesional or remote regions inside the ipsilesional half of the cerebrum or of contra-hemispheric homologous regions. The integration these concepts into therapeutic methods brought out dramatic updates in the management of DLGG, with an increase of surgical intervention in eloquent areas traditionally believed as untouchable [(1)].

Currently, the role of biopsy is very narrow in DLGG. As combining clinical and radiological data, the diagnosis of glioma is typical in majority of cases. So, the aim of neuropathological examination was to identify the actual grade of the glioma. But, there is a high risk of sampling error. ***Muragaki el al.*** [(2)] showed that upgrading of WHO grade I gliomas occurred in 11% of cases and downgrading of WHO grade III gliomas in 28%.

Conversely, maximal DLGG resection provided more amount of tissue, leading to increase in the reliability of
the histopathological diagnosis and grading. Also, biopsy has no therapeutic role [(2)]. Depending on these oncological results, the strategy of management should be moved toward operating the nervous system involved by a chronic oncological disease and not a mass any more. As the target is not to remove apart from the tumor visible on imaging studies, but to do the most possible extensive resection of the tissue invaded by DLGG, provided that this is not effecting functions. Thus, neurosurgeon should aim the procedure to the individual cerebral anatomical and functional organization, as procedure within the cerebrum has to be different from the any procedures outside the cerebrum. A corner stone in glioma surgery should be to tailor the resection on functional boundaries, with no margin, to maximize the tumor removal while protecting eloquent areas [(3)].

## AIM OF THE STUDY

This study aimed to evaluate the risk and benefit of maximizing the extent of resection of



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diffuse low grade Glioma even in the functional cortex that has been traditionally believed to be too risky to remove as regards; preserving neurological function with maximum resection.

## SUBJECTS AND METHODS

### Study design:

This was a prospective observational study for 20 consecutive patients, whom underwent surgery for Diffuse Low grade glioma at Ain Shams University Hospitals for planning for maximal tumor resection even if presuming the proximity of these lesions to eloquent cortex and their relative diffuse nature on imaging.

**The study was approved by the Ethics Board of Ain Shams University.**

## METHODOLOGY

### A. Patient selection:

**Inclusion Criteria***:* 18 years and over, both genders were eligible for this study. Performance status was Karnofsky Scale varied from 60-100% and with an initial imaging diagnosis of supratentorial WHO grade II astrocytoma (Diffused fibrillary, protoplasmic, or gemistocytic), oligodendroglioma and oligoastrocytoma.

**Exclusion Criteria***:* patients with recurrent gliomas, brainstem lesions, insular lesions, patients with contraindications for MRI, patient who was received chemo or radiotherapy for brain lesions.

**B. Patient assessment*:*** each patient was initially neurologically preoperative assessed within one week before surgery; Measurement of performance status was done using Karnofsky Performance Scale (KPS). All patients enrolled in this study underwent preoperative MRI with contrast. MR Diffusion Tensor Image (DTI) and Functional MRI "fMRI" were carried out for the eloquent area lesions and the tractographic data were evaluated and employed in the neurosurgical planning. The goal was maximal safe resection of signal abnormality defined on MRI T2/FLAIR, in whom maximal tumor resection was likely to be achieved at the time of surgery.

**C. Procedure***:* standard operative procedures included intraoperative visualization tools "including ultrasound and/or neuro-navigation system "and monitoring tools may be used according to the site of the lesion and its feasibility. fMRI and MRI DTI information regarding the intra-axial lesion close to eloquent area and tracts were used in the preoperative surgical planning.

**D. Postoperative and outcome evaluation*:*** each patient was neurologically assessed within the first 72 hours and before discharge from hospital, the post-operative MRI was obtained within 72 hours included a volume T2 and FLAIR sequence to evaluate extent of resection in volumetric analysis. Extent of resection was expressed as Gross Total (GTR): no residual by follow up MRI, Subtotal (STR): resection of > 75% and less than 100%, Partial (PR): less than 75%. The EOR was calculated as follows: preoperative tumor volume - postoperative tumor volume /preoperative tumor volume. Final pathology results were compared with the pre-operative and intraoperative (if done) provisional diagnosis. After discharge patients was followed up at least 6 months. During follow up patients was evaluated regarding seizures control, neurological examination, current Karnofsky Performance Scale. Also during follow up patients had consecutive MRI brain studies.

### *Statistical Analysis*

Statistical significance was set at P value of 0.05. All statistical calculations were run using SPSS version 22.

## RESULTS

Study period was almost 30 months, from 1/3/2013 till 1/9/2015, when there were no new patients to be enrolled in the study. Total number of study enrolled was 20 patients. Male (65%): Female (35%) Ratio 1.8:1 (n=13:7), Patient's age, range: 21 years – 59 years, average: 39.3, SD 11.86. Positive Family history of brain tumor was 20% (n=4). Presenting manifestation was seen in the study cohort (**Figure 1)**. Sick leaves were in 70%, ranged from 1 to 21 days, average was 2 days. Pre-operative deficits were found in 50% of patients (n=10) presented as follow: motor deficit was 30%, motor deficit aesthesia 5%, dysarthria 5% and dysphasia 5%.

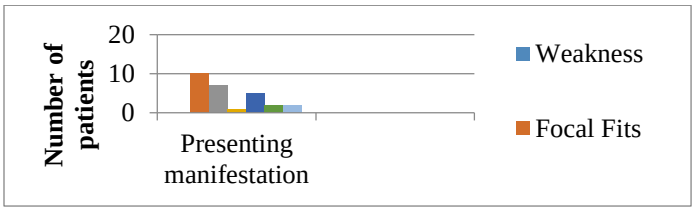


**Figure 1: presenting manifestation in the studied cohort**

GTR was achieved in 10%, STR in 65% and PR in 25%. Postoperative deficit after 72-hours showed that deficit was 75% presented as follow (n=15): Motor deficit was 60%, aesthesia 5%., dysarthria 5% and dysphasia 5%. 25% of patients developed new

postoperative deficit. Before discharge from hospital it was the same as 72-hour postoperative except motor deficit improved in 2 patients. During the follow-up at the first 6-month post-operative, 1 patient died (5%), 2 patients (10%) with motor weakness and 17 patients (85%) showed no deficit from the study cohort. After 6 months post-operative assessment showed only 1 patient (5%) with motor deficit. There was no post-operative morbidity in 80% of the cases, which required prolonged hospital stay or re-hospitalization or discharge to rehabilitation center. Intraventricular hemorrhage occurred in 1 patient and resolved in 9 days before discharge and no consecutive hydrocephalus seen during follow-up period up to till 1 year. Urinary tract infection, which required hospital re-admission, was seen in 1 patient, 2 weeks postoperative. Only in 1 patient, motor weakness grade 4 according to MRC was still present and not improving "residual deficit after 6 months", which considered the only mortality in the study cohort. While, the mortality was seen only in 1 patient whom died 10 weeks post-operative. There was mortality and morbidity within the first 6 months of follow-up postoperative, seen in near eloquent group 15%. After 6 months, only 1 mortality 5% and 1 morbidity 5%, which represent 10% of study cohort in near eloquent group. For post-operative morbidity in STR group 5% motor weakness, 5% IV hemorrhage and 5% urinary tract infection. PR had 5% mortality in second month poet-operative. While, GTR showed neither mortality nor morbidity. Morbidity and mortality after 6 months: only 1 case was detected in STR group (5% of all studied cohort). One patient died in PR group (5% of all study cohort). LOS at hospital post-operative was 15 days in average (4-19 days). LOS was the longest (4-16 days) in near eloquent and shortest in eloquent (5-8 days), while in non-eloquent it varied from 4-11 days. Functional outcome was shown in **table 1.**

**Table 1: patient outcome**

| # | Pre-perative Deficit | Post-perative Deficit | OS | Deficit within 6 months | Deficit after 6 months | k Leave | KPS eoperative | postop PS 72hr | KPS ithin 6 months | PS after months | CS pre-perative | CS post-perative 2 hours | GCS ithin 6 mon | ack to work |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ysphasia | sphasia | 6 | no | no | 1 | 90 | 50 | 90 | 100 | 15 | 15 | 15 | 4 |
| 2 | G4 | G4 | 5 | no | no | 4 | 80 | 60 | 90 | 100 | 15 | 15 | 15 | 2 |
| 3 | G4 | G4 | 8 | no | no | 2 | 70 | 60 | 90 | 100 | 15 | 15 | 15 | 1 |
| 7 | G4 | G4 | 14 | no | no | 7 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 3 |
| 5 | G4 | G4 | 5 | no | no | 4 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 4 |
| 6 | ysarthria | sarthria | 4 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 2 |
| 4 | no | no | 5 | no | no | 1 | 90 | 80 | 100 | 100 | 15 | 15 | 15 | 2 |
| 8 | ypothesia | pothesia | 5 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 3 |
| 9 | G3 | G4 | 6 | G4 | no | 1 | 100 | 60 | 90 | 100 | 15 | 15 | 15 | 2 |
| 10 | no | no | 8 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 2 |
| 11 | G4 | G4 | 5 | no | no | 1 | 80 | 70 | 90 | 100 | 15 | 15 | 15 | 3 |
| 12 | G4 | G4 | 6 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 1 |
| 13 | no | no | 5 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 1 |
| 14 | G0 | CL, G0 | 19 | dead | dead | 1 | 90 | 30 | Dead | Dead | 15 | 12 |  | Dead |
| 15 | no | no | 11 | no | no | 1 | 90 | 70 | 100 | 100 | 15 | 15 | 15 | 1 |
| 16 | G3 | G3 | 11 | no | no | 3 | 80 | 70 | 90 | 100 | 15 | 15 | 15 | 3 |
| 17 | no | no | 4 | no | no | 1 | 100 | 70 | 100 | 100 | 15 | 15 | 15 | 1 |
| 18 | G2 | G4 | 16 | no | no | 4 | 90 | 40 | 100 | 100 | 15 | 14 | 15 | 3 |
| 19 | G4 | no | 11 | no | no | 1 | 90 | 60 | 100 | 100 | 15 | 14 | 15 | 2 |
| 20 | G4 | G2 | 14 | G$ | G4 | 21 | 80 | 70 | 90 | 100 | 15 | 15 | 15 | 4 |

Regarding seizures, preoperative seizures were seen in 70% of cases. 25% was focal, 20% GTC and focal with secondary generalization in 25%. Preoperative seizures were not controlled in 50% when seizures were found. While post-operative seizures were found in 20% early post-operative, which was controlled either by increasing the dose of AED in 5% and adding another AED in 15%. Before 6 months post-operative seizures were seen in 15%, and 5% after 6 months. AEDs were stopped before year in 45% of the cases, 50 not stopped till year of follow-up and one patient died 5%. Six cases (30%) had pre-operative uncontrolled seizures, which showed no seizures post-operative, half of them stopped the AED within a year. Six cases (30%) had not pre-operative seizures and did not have seizures post-operative, 5 stopped the AED at one year and 1 at 4 months. Four cases (20%) had pre-operative controlled seizures, and no seizures post-operative both stopped AED at 6 months and the other at 1 year. Three cases (15%) had pre-operative controlled seizures, which were controlled before 6-months post-operative, 1 of them stopped the AED at 6 months. One case (5%) had uncontrolled seizures which was not controlled till 6-month post-operative. EOR when correlated to number of AED post-operative, P value was 0.5: All patients who had GTR did not need more than one AED. STR 11/13 had one AED and 2/13 had two AED needed to be controlled. In PR group 80% were on 1 AED and 20 % were on 2 AED. Seizures occurrence correlated to EOR during the first 6-months post-operative, P value was 0.1: 50% of GTR, 18.2 % of STR and 0% of PR. AED stoppage when compared to EOR: Stopped in 55% of study cohort, average 10.72 months(n=11): STR 72.7% (8/11), PR 18% (2/11), GTR 9% (1/11) and Continued in 45% (n=8+1 died) for more than 1 year. Sick leaves; When there were seizures (40%) sick leave was shorter: In GTC it was one day, focal with secondary generalization it varied from 2-7 days, focal was from 1 to 21 days and when there were no seizures (60%) it varied from 1-21 days.

EOR correlated to outcome seen in **table 2**.

**Table 2: EOR vs outcome**

| # | Final Pathology | Pre-op Deficit | KPS re-op | Pre-op Tumor Volume | EOR | EOR % | Residual deficit | KPS at months | Back to work | Complications | Need for another surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | Astrocytoma G2 | no | 90 | 31.03 | Partial | 0.61 | no | 100 | 4 | no | no |
| **2** | Oligoastrocytoma G3 | yes | 80 | 19 | Partial | 0.42 | no | 100 | 2 | no | no |
| **3** | Oligodendroglioma G2 | yes | 70 | 160.22 | STR | 0.85 | no | 100 | 1 | no | no |
| **7** | Hashimoto's encephalopathy | yes | 90 | 2.26 | GTR | 1 | no | 100 | 3 | no | no |
| **5** | Oligoastrocytoma G2 | yes | 90 | 45.6 | STR | 0.92 | no | 100 | 4 | no | no |
| **6** | Oligodendroglioma G2 | yes | 90 | 12.93 | STR | 0.93 | no | 100 | 2 | UTI | no |
| **4** | Oligodendroglioma G2 | no | 90 | 86.81 | STR | 0.85 | no | 100 | 2 | no | no |
| **8** | Oligodendroglioma G2 | yes | 90 | 84.67 | Partial | 0.46 | no | 100 | 3 | no | no |
| **9** | Oligodendroglioma G2 | no | 100 | 39.06 | STR | 0.71 | no | 100 | 2 | no | no |
| **10** | Oligodendroglioma G2 | no | 90 | 42.73 | STR | 0.95 | no | 100 | 2 | no | no |
| 11 | Astrocytoma G2 | no | 80 | 35.71 | STR | 0.93 | no | 100 | 3 | no | yes |
| 12 | Oligoastrocytoma G3 | no | 90 | 99.5 | STR | 0.83 | no | 100 | 1 | no | no |
| 13 | Oligodendroglioma G2 | no | 90 | 1.1 | GTR | 1 | no | 100 | 1 | no | no |
| 14 | Oligodendroglioma G2 | no | 90 | 18.5 | Partial | 0.62 | dead | dead | dead | dead | no |
| 15 | Astrocytoma G2 | no | 90 | 46.92 | STR | 0.89 | no | 100 | 1 | IV hemorrhage | no |
| 16 | Oligoastrocytoma G3 | no | 80 | 50 | STR | 0.85 | no | 100 | 3 | no | no |
| 17 | Oligodendroglioma G2 | no | 100 | 9.98 | STR | 0.95 | no | 100 | 1 | no | no |
| 18 | Central Neurocytoma | yes | 90 | 46.5 | Partial | 0.34 | no | 100 | 3 | no | no |
| 19 | Astrocytoma G2 | no | 90 | 32.2 | STR | 0.77 | no | 100 | 2 | no | no |
| 20 | Oligoastrocytoma G3 | yes | 80 | 51.23 | STR | 0.79 | yes | 100 | 4 | G4 weakness | no |

From this study cohort, rehabilitation was only needed in 10% who received speech therapy and 50% physiotherapy. 50% of GTR needed physiotherapy, 46.1% of STR and 60% of PR. Only 40% of PR required

speech therapy. 50 % from who had motor deficit post-operative cured on physiotherapy, except 1 died and the other 1 had his motor power improved from G2 to G4+ at 6 months, all lesions were close to motor area. 50 % from who had speech deficit post-operative improved on speech therapy, 1 died (SMA syndrome) and the other 1 had his lesion in speech center, dysphasia improved after 3 months gradually. Recommendation for another surgery for residual lesion was only in 1 case in STR group 5%. Only 35% of the cases received RT, one cases refused, and one case clinical condition was not fit to undergo RT.60% of the cases received chemotherapy, 35% before RT for radio-sensitization. Regarding pathology, in all cases when positive family history for brain tumor was found, 1p19q co-deletion also was found to be positive (n=4) 20%. Provisional surgeon diagnosis matched final Pathology and radiological diagnosis both in 13/20 65%. Provisional radiological diagnosis matched final Pathology in 15/20 75% (P value=0.3). The 5 unmatched were: 1 central neurocytoma in 1 encephalitis, 3 oligoastrocytoma G3. Provisional surgeon diagnosis matched final Pathology in 14/20 70% (P value = 0.7). The 6 unmatched were:1 cavernoma, 1 oligodendroglioma and 4 G2. While, fMRI when done (65%) and was positive (25%), EOR PR in 10%, STR 10% and GTR 5%. When was negative, STR was 30% and 10% PR. EOR when correlated to DTI showed that STR was feasible in 25% where CST was shifted without disrupting, and 5% when was disrupting. PR was feasible in 15% when CST was shifted without disrupting and 5% when was disrupting. GTR was feasible in 5% when there was no interruption of CST or displacement. EOR correlations when dominance compared to EOR; GTR was achieved in non-dominant sides only 2/11. STR was achieved in 6/9 in dominant side and 7/11 in non-dominant. PR was achieved in 3/9 when lesion was on dominant side and 2/11 when was non-dominant. When location compared to EOR; GTR was only seen when the lesion was in frontal lobe in both 2 cases when achieved. STR was seen in all other lobes and PR was seen in frontal lobe mainly and one case was temporal. When eloquence compared to EOR: Dominant side and eloquent was Partial Resection (PR) (15%) and Subtotal Resection (STR) (15%). Dominant side and near eloquent was STR (15%). Non-dominant side and non-eloquent it was STR (25%) and Gross Total Resection (GTR) (5%). Non-dominant side and near eloquent was STR (10%), PR (10%) and GTR (5%). When lesion was near to motor area, EOR was PR (2/7) and STR (5/7). When lesion was close to Supplementary Motor Area (SMA), EOR was GTR 100%. When lesions were in motor area PR seen 100%. When lesion was in speech area PR was seen in 50% and STR 50%. For non-eloquent EOR were STR 5/6 and GTR 1/6. Intraoperative tools were compared to EOR was shown in **table 3**.

**Table 3: EOR and intraoperative techniques correlation**

| | | Intraoperative techniques | | | | |
|---|---|---|---|---|---|---|
| | | Stereotactic navigation | Stereotactic navigation, Frozen, EEG, Electrophysiological monitoring | Stereotactic navigation, Frozen, iMRI, EEG, Electrophysiological monitoring | Stereotactic navigation, Frozen, iMRI, EEG, Electrophysiological monitoring and awake | Stereotactic navigation, Ultrasound |
| EOR Quality | GTR | 0 | 1 | 1 | 0 | 0 |
| | Partial | 0 | 2 | 2 | 0 | 1 |
| | STR | 2 | 1 | 9 | 1 | 0 |
| Total | | 2 | 4 | 12 | 1 | 1 |

## DISCUSSION

Managing tumors or lesions of diffused low grade nature is a subject of growing interest and we hope that the data provided by the current study serve as a guide through some controversial issues. As outlined in the methodology and results sections, this study was done in

a prospective fashion and is a tertiary care facility with full set up and preparedness for microsurgical approaches and full radiological studies if necessary. There was slight male predominance in the enrolled patients, mean age of 39.9 years with a wide range (21 years – 59 years). As mentioned in literature, it usually affects young adults between age 30 - 40.(4), typically affecting younger persons (median age 35) and mainly males (male/female ratio 1.5)(5,6) As expected, seizures were the commonest presenting manifestation, being found in 60% (n=12) of the patients. Young adults usually present with epilepsy and without any neurological deficit (often partial seizures).(7) Headache (30%, n=6) ranking as the next common presentations, motor weakness (5%, n=1) and sensory (5%, n=1). Incidental finding was (10%, n=2). Headache, personality changes, and focal neurologic deficits are representing the other most common symptoms. The other neurologic symptoms are motor/sensory deficits, dysphasia/aphasia, disinhibition, apathy and visuospatial disturbances according to tumor location and size [8]. Provisional radiological diagnosis matched surgeon's provisional "assumption" diagnosis based on radiological studies and clinical presentation (95%, n=19). While, provisional radiological diagnosis matched proved final pathology in (75%, n=15). Surgeon's provisional "assumption" diagnosis matched proved final pathology in (70%, n=14). Four cases were assumed as low grade lesion and proved to be high grade, while one was suspected to be low grade glioma and final results found to be encephalitis and the other case was central neurocytoma. The molecular profile of oligodendrogliomas is the combined loss of 1p/19q occurring in 70%–80% of these tumors, which is associated with longer survival[9]. In our study, 1p/19q co-deletion assay was positive when done in 64.7%; 7/9 of oligodendroglioma G2, 2/4 Astrocytoma G2, 1/1 Oligoastrocytoma and 1/1 oligodendroglioma G3. In the recent WHO classification diagnosis of oligodendroglioma and anaplastic oligodendroglioma requires demonstration of an IDH mutation and 1p/19q co-deletion. Currently oligodendroglioma is essentially defined by this genetic phenotype [10,11]. In our study, 45% of lesions located in dominant hemisphere. 40 % were near eloquent area, 30 % were at eloquent areas and 30% located at non-eloquent and not close to eloquent areas, 35% of tumors were close to motor area, 5% at motor area, 5% close to SMA, 20% at speech area and 5% at somatosensory area. Our finding are close to results seen in many studies where 82.6% of tumors were located within eloquent motor or language areas (27.3% of cases within the SMA, 25.0% in the insula, 18.9% in language centers, 6.0% in the primary somatosensory area, 4.5% in the primary motor area) [3,12]. Functional MRI was done in 65% of our cases and not needed in 35% of cases. When done it was positive in 25% of the cases and negative in 40 %. Regarding validation of fMRI, several studies reported a good correlation between fMRI and intraoperative monitoring. **Majos *et al.*** [13] compared preoperative fMRI findings with DES in 33 patients with Rolandic brain lesions and they found 83% matching for the motor cortex and 83% agreement for the somatosensory cortex between the two techniques. The match increased to 98% when both types of activation were taken into consideration. DTI was done in 55% of the cases, all of the studies were done to study corticospinal Tract (CST) in relation to the lesion; 40 % of the cases CST was shifted without disrupting, 10% shifted and disrupting and 5% there was no interruption or displacement of the tract. Recently **Zetterling** and his colleagues proved that DTI is an accurate tool for detection of infiltrative nature lesions such as DLGGs and possibility improve radical resection and avoidance of postoperative morbidity and outcome [14]. MR spectroscopy was done in 30% of patient and matched the final diagnosis in all of them. Interestingly that it was not done in central Neurocytoma and encephalopathy lesions. While tumors typically exhibit elevated Cho and decreased NAA, the greatest value of adding MRS is including or excluding diagnoses with markedly other different pathologies with different spectroscopic patterns, such as strokes, or focal cortical dysplasia [15].Intraoperative MRI may allow for greater EOR especially when tumor-infiltrated tissue cannot be grossly differentiated from normal surrounding tissue [16]. In our study intraoperative MRI was used in 65% of cases, all of them achieved STR and 1 case GTR. **Duffau *et al.*** [3] compared EOR vs functional outcome "KPS", for a total of 12 resections, GTR was achieved in 6 and STR in the other 6 cases (there were no cases of PR), the mean follow-up period postoperative was 46 months. There was no mortality or severe permanent neurological due to the surgeries. Surgery aimed to maximal resection of lesions and preservation of brain function. A wake surgery with intraoperative functional brain mapping was performed. All patients returned to their normal social and professional life and all had a KPS score of 90 or 100 at the most recent follow-up. They concluded that intraoperative mapping with functional guided excision may allow safe resection while maximizing the extent of resection in DLGGs[6]. In our study, we focused the analysis on functional outcome after surgery among the newly diagnosed DLGGs, excluding any patient how received RT or Chemotherapy or biopsy. Our results showed that better "higher" KPS at diagnosis is a

predictive factor for early improvement of KPS during the first 6 months P value =0.9. Post-operative KPS 72 hours varied from 30 to 80, when the lesion was not eloquent. While, near to eloquent was 30 – 70 when the lesion were eloquent 50 - 70. In the studied cohort 60% were 70, 20% were 60, 5% were 30, 40, 50 and 80 each. Post-operative KPS at 6 months was 100 for 95% except for one patient 5% who passed away post-operative during 2nd month of follow-up. While **Yeh *et al.*** showed that EOR and postoperative KPS are independent prognostic factor for OS using multivariate analysis in 93 consecutive DLGGs [17]. In all recent case series with objective postoperative evaluation of EOR on T2/FLAIR-MRI, more aggressive excision predicted a significant improvement in OS compared with simple excision. When no signal abnormality was visible on follow up MRI (GTR), patients had a significantly longer OS when compared to patients having any residual signal abnormality. Also in STR with a residual tumor volume less than 10 ± 5cc), patients with a greater percentage of resection had a significantly better (longer) OS.[18] The surgery delayed histological upgrading, as the volume of residual tumor mass serves as a strong predictor of anaplastic transformation. There is a cumulative evidence that GTR at initial surgery represents a strong prognostic factor[19] ,even in cases of incomplete excision, as extensive tumor excision patients had significantly longer OS[20]. To summarize, early and maximal surgical resection is the first therapeutic option currently to consider in DLGG, as concluded by the European guidelines [21].To the best of our knowledge, the EOR leads to significantly longer OS [14,15,20,22,23] . Surprisingly supra-total resection for DLGGs was recommended, of a margin around the signal abnormality in non-eloquent areas which could improve OS by decreasing malignant transformation [24]. There was mortality within the first 6 months of follow-up post-operative, seen in near eloquent group in the second month postoperative, a single case 5% belongs to PR group. For post-operative morbidity in STR group 5% motor weakness, 5% IV hemorrhage and 5% urinary tract infection. While, GTR showed neither mortality nor morbidity. After 6 months only one case 5% had G4 weakness which improved from G3 immediate postoperative. The postoperative functional compensation could be due to brain plasticity. Indeed, the immediate post-operative deficit observed in many patients confirmed that some structures remain functional within the tumor mass or peri-tumoural tissue because this deficit cannot be explained by a simple edema as it was a chronic lesion in its nature, in spite of a possible pre-operative loco-regional reshaping due to DLGG. Immediately postoperative the peri-tumoural tissue reorganization fail to keep sufficient function in addition to the fact of this reorganized brain tissue around the tumor cavity has been temporarily damaged by the procedure itself. The occurrence of deficit was higher in patients with already pre-existing motor or language deficit and most of the neurological deficits were transient and disappeared within 1 month from surgery. This agrees with our results as patients with pre-existing motor deficit had more eventful post-operative course, 40% of patients had preoperative deficit, 75% immediate post, 10% within the first 6 months and 5% after 6 months [25].The effect of surgical resection for DLGGs on the occurrence of seizures has been well documented by many authors. As seizures play an important role in postoperative quality of life of patients who undergo surgical resection of DLGGs. Half of patients had a seizure at time of diagnosis and more than 81% had seizures persist after diagnosis even under AEDs treatment. Cortical lesions, oligodendroglioma and oligoastrocytoma were significantly more likely to produce seizures when compared to deeper locations and astrocytoma. Regarding seizures control in our study we positively support such pervious findings as 30% had pre-operative uncontrolled seizures, which showed no seizures post-operative, half of them stopped the AED within a year. 30% had not pre-operative seizures and did not have seizures post-operative, 5 stopped the AED at one year and 1 at 4 months. 20% had pre-operative controlled seizures, and no seizures post-operative both stopped AED at 6 months and the other at 1 year. 15% had pre-operative controlled seizures, which were controlled before 6-months post-operative, 1 of them stopped the AED at 6 months. Only single case (5%) had uncontrolled seizures which was not controlled till 6-month post-operative. While, EOR when correlated to number of AED post-operative, all patients who had GTR did not need more than one AED, STR 11/13 had one AED and 2/13 had two AED to be controlled. In PR group 80% were on 1 AED and 20 % were on 2 AED. Only one case was offered surgery again for the same pathology from the STR group in our study. In literature re-resection seems to provide significant benefit, and EOR remains the strongest predictor of OS [25].

## CONCLUSION

Stand-alone surgical resection can be a trustable initial step in the treatment for resection of diffuse low-grade gliomas according to strict pre-surgical planning. Careful pre-surgical planning based on proper history reviewing, recent imaging techniques and utilizing up-to-date intra-operative technology is helping to maximize safe surgical resection while saving patient function and quality of life. The operative success achieved by these

techniques provides efficient symptomatic control of the patients' presentation in most of the cases. The safety profile of this technique is comparable to the conventional other techniques for management of this kind of lesions, when comparing benefits to risks. Further studies are still needed with larger study cohort and long-term follow-up.

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