Tratamento Atual dos Gliomas de Baixo Grau

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Outline

• HCor Neurociência
• Pre-operative Planning
• Surgical Strategy and Phylosophy
• Stereotactic Radiation
• Adjuvant Chemotherapy
• Future Trials

“The future belongs to the ones that can follow their dreams.”
Roosevelt
2008 – Escolha do Local

15% of the American Population have access to Trials
Pre-operative Exams

- MRI
- Bold
- Angio
- PET
- TMS Navigation – Mapping

Planned resection and radiation:

- Adaptive Hybrid Surgery
- In Room Plan of Radiosurgery

Decrease Surgery Side Effects
Decrease Radiation Side Effects
Imaging Improvement

Image Fusion - 2001

3D Image - 2008
Microdrive

Anestesia

Neurologista

Microdrive
Objective: The purpose of this study was to evaluate the feasibility of microelectrode recording, electrical stimulation, and electrode position checking during functional neurosurgical procedures (DBS, lesion) in the interventional magnetic resonance imaging (iMRI) environment. Methods: Seventy-six surgical procedures for DBS implant or radiofrequency lesion were performed in an open 0.2 T MRI operating room. DBS implants were performed in 54 patients (72 surgical procedures) and unilateral radiofrequency lesions in three for a total of 76 surgeries in 57 patients. Electrophysiological studies including macrostimulation and microelectrode recordings for localization were obtained in the 0.5 to 10 mT fringes of the magnetic field in 51 surgeries. MRI confirmation of the electrode position during the procedure was performed after ... Symptomatic hemorrhage was detected in two (2.6 %) patients during the operation. Image quality of the 0.2 T MRI scan was sub-optimal for anatomical localization. However, image fusion with pre-operative scans permitted excellent visualization of the DBS electrode tip in relation to the higher quality 1.5 T MRI anatomical scans. Conclusion: This study shows that conventional stereotactic localization, microelectrode recording, electrical stimulation, implant of DBS hardware, and radiofrequency lesion placement are possible in the open 0.2 T iMRI environment. The convenience of having an imaging modality that can visualize the brain during the operation is ideal for stereotactic procedures.
Deep brain stimulation in intraoperative MRI environment - comparison of imaging techniques and electrode fixation methods.

Lee MW, De Salles AA, Frighetto L, Torres R, Behnke E, Bronstein JM.

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We performed 118 consecutive DBS cases from November 1999 to June 2002. Intraoperatively there were 10 cases studied with fluoroscopy, 73 with 0.2 Tesla (T) MRI and 35 with 1.5 T MRI. Ten electrodes were secured by Medtronic caps, 25 by methyl methacrylate with titanium miniplates, and 82 by Navigus caps. The 3-dimensional displacement between the planned target and actual electrode position (3DD) was determined by fusing the postoperative MRI with the preoperative imaging. The 3DD for using Medtronic caps, methyl methacrylate with miniplates, and Navigus caps were 4.80 +/- 3.16, 2.64 +/- 1.26 and 2.23 +/- 1.15 mm (mean +/- SD), respectively. Navigus caps had statistically significant accuracy (P = 0.03) in holding the electrode when compared with Medtronic caps, and it facilitated electrode revision. The fixation devices significantly affect the final vertical position of the electrode. The 3DD for fluoroscopy, 0.2 T and 1.5 T MRI cases were 4.80 +/- 3.16, 2.31 +/- 1.21 and 2.34 +/- 1.14 mm (mean +/- SD), respectively. No statistically significant difference (P = 0.91) in 3DD was demonstrated between 0.2 T and 1.5 T MRI cases. The presence of intraoperative 1.5 T MRI allowed near real-time electrode position confirmation and early detection of hemorrhagic complications. Satisfactory microelectrode recording was feasible in low-field 0.2 T and high-field 1.5 T MRI environments. Further studies on performing DBS in real-time intraoperative MRI are warranted.
A role of diffusion tensor imaging in movement disorder surgery.

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The safe and reversible nature of deep brain stimulation (DBS) has allowed movement disorder neurosurgery to become commonplace throughout the world. Fundamental understanding of individual patient's anatomy is critical for optimizing the effects and side effects of DBS surgery. Therefore, at the institution's intraoperative magnetic resonance imaging operating theater (BrainLAB), stereotactic targets and fiber tractography were determined on preoperative magnetic resonance imagings using the Schaltenbrand-Wahren atlas for definition in the BrainLab iPlan software (BrainLAB Inc., Feldkirchen, Germany). Subthalamic nucleus, globus pallidus interna, and ventral intermediate nucleus targets were studied.

Diffusion tensor imaging parameters used ranged from 2 to 8 mm for volume of interest in the x/y/z planes, fiber length was kept constant at 30 mm, and fractional anisotropy threshold varied from 0.20 to 0.45. Diffusion tensor imaging tractography allowed reliable and reproducible visualization and correlation between frontal eye field, premotor, primary motor, and primary sensory cortices via corticospinal tracts and corticopontocerebellar tracts. There is an apparent increase in the number of cortical regions targeted by the fiber tracts as the region of interest is enlarged. This represents a possible mechanism of the increased effects and side effects observed with higher stimulation voltages. Currently available diffusion tensor imaging methods to characterize the effects and side effects of DBS. This technology has the potential of being a powerful tool to optimize DBS neurosurgery.
Shields DC, Gorgulho A, Behnke E, Malkasian D, DeSalles AA.

Division of Neurosurgery, Department of Surgery, David Geffen School of Medicine, University of California, Los Angeles, USA.

OBJECT: Deep brain stimulation of the subthalamic nucleus (STN) in patients with Parkinson disease is often very effective for treatment of debilitating motor symptoms. Nevertheless, the small size of the STN and its proximity to axonal projections results in multiple side effects during high-frequency stimulation. Contralateral eye deviation is produced in a small percentage of patients, but the precise mechanism of this side effect is at present poorly understood. METHODS: Contralateral eye deviation was produced by high-frequency stimulation of 22 contact sites in nine patients undergoing deep brain stimulation of the STN. The precise locations of these contacts were calculated and compiled in order to locate the stimulated structure responsible for eye deviation. The mean x, y, and z coordinates associated with contralateral eye deviation were found to be 11.57, 2.03, and 3.83 mm lateral, posterior, and inferior to the anterior commissure-posterior commissure midpoint, respectively. The point described by these coordinates is located within the lateral anterosuperior border of the STN. CONCLUSIONS: Given that stimulation of frontal eye field cortical regions produces similar contralateral conjugate eye deviation, these results are best explained by electrical current spread to nearby frontal eye field axons coursing lateral to the STN within the internal capsule. Thus, placement of the implanted electrode in a more medial, posterior, and inferior position may bring resolution of these symptoms by reducing the amount of current spread to internal capsule axons.
Stereotactic coordinates associated with facial musculature contraction during high-frequency stimulation of the subthalamic nucleus.

Gorgulho AA, Shields DC, Malkasian D, Behnke E, De Salles AA.

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OBJECT: High-frequency stimulation of the subthalamic nucleus (STN) in patients with parkinsonian symptoms is often used to ameliorate debilitating motor symptoms associated with this condition. However, this relatively small nucleus results in multiple side effects related to the spread of electrical current to surrounding structures. Specifically, contraction of the muscles of facial expression is noted in a small percentage of patients, although the precise mechanism remains poorly understood.

METHODS: Facial muscle contraction was triggered by high-frequency stimulation of 49 contacts in 18 patients undergoing deep brain stimulation of the STN. The mean coordinates of these individual contacts relative to the anterior commissure-posterior commissure midpoint (also called the midcommissural point) were calculated to determine the location or structure(s) most often associated with facial contraction during physiological macrostimulation.

RESULTS: The x, y, and z coordinates associated with contraction of the facial musculature were found to be 11.52, 1.29, and 1.15 mm lateral, posterior, and inferior to the midcommissural point, respectively. This location, along the lateral-anterior-superior border of the STN, may allow for the spread of electrical current to the fields of Forel, zona incerta, and/or descending corticospinal/corticobulbar tracts. Because stimulation of corticobulbar tracts produces similar findings, these results are best explained by the spread of electrical current to nearby internal capsule axons coursing lateral to the STN.

CONCLUSIONS: Thus, if intraoperative deep brain stimulation lead testing results in facial musculature contraction, placement of the electrode in a more medial, posterior position may reduce the amount of current spread to corticobulbar fibers and resolve this side effect.
The role of modern imaging modalities on deep brain stimulation targeting for mental illness.

**Sedrak M, Gorgulho A, De Salles AF, Frew A, Behnke E, Ishida W, Klochkov T, Malkasian D.**

Division of Neurosurgery, David Geffen School of Medicine, University of California Los Angeles (UCLA), Los Angeles, CA, USA.

INTRODUCTION: The reversible nature of deep brain stimulation (DBS) brought renewed interest on surgically treating medically intractable mental illnesses. The explosion of anatomical and functional imaging has allowed the development of new potential targets and the understanding of historical targets. METHODS: Fifteen patients undergoing stereotactic surgery for movement disorders at UCLA's interventional MRI operating-room were studied with fiber tracking. Stereotactic targets and fiber tracking were determined on MRIs using the Schaltenbrand-Wahren atlas for definition in the iPlan software. DTI parameters used ranged from 10 to 20mm for voxel size in the x/y/z planes, fiber length was kept constant at 36 mm, and fractional anisotropy (FA) threshold varied from 0.20 to 0.25. RESULTS: Reliable interconnectivity of targets was determined with DTI and related to PET imaging. Mental illness targets were observed with functional and fiber tract maps. This confirmation yields reliability to DTI imaging in order to determine novel targets and enhance the understanding of areas not well understood.

CONCLUSIONS: Currently available imaging techniques, the reversibility of DBS to modulate targets promises to bring a brighter future for surgery of mental illness.
Potential surgical targets for deep brain stimulation in treatment-resistant depression

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Object. The goal of this study was to evaluate the definition of treatment-resistant depression (TRD), review the literature regarding deep brain stimulation (DBS) for TRD, and identify potential anatomical and functional targets for future widespread clinical application.

Methods. A comprehensive literature review was performed to determine the current status of DBS for TRD, with an emphasis on the scientific support for various implantation sites.

Results. The definition of TRD is presented, as is its management scheme. The rationale behind using DBS for depression is reviewed. Five potential targets have been identified in the literature: ventral striatum/nucleus accumbens, subgenual cingulate cortex (area 25), inferior thalamic peduncle, rostral cingulate cortex (area 24a), and lateral habenula. Deep brain stimulation electrodes thus far have been implanted and activated in these structures in humans. These targets have proven to be safe and effective, albeit in a small number of cases.

Conclusions. Surgical intervention for TRD in the form of DBS is emerging as a viable treatment alternative to existing modalities. Although the studies reported thus far have small sample sizes, the results appear to be promising. Various surgical targets, such as the subgenual cingulate cortex, inferior thalamic peduncle, and nucleus accumbens, have been shown to be safe and to lead to beneficial effects with various stimulation parameters. Further studies with larger patient groups are required to adequately assess the safety and efficacy of these targets, as well as the optimal stimulation parameters and long-term effects. (DOI: 10.3171/FOC/2008/25/7/E3)

KEY WORDS • deep brain stimulation • depression • psychosurgery
Incidence of hemorrhage associated with electrophysiological studies performed using macroelectrodes and microelectrodes in functional neurosurgery

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Infection following deep brain stimulator implantation performed in the conventional versus magnetic resonance imaging–equipped operating room

Clinical article

ALESSANDRA GORGULHO, M.D.,1 CATHERINE JUILLARD, M.D.,1 DANIEL Z. USLAN, M.D.,2 KATAYOUN TAJIK, B.S.,1 POORANG AURASTEH, B.S.,1 ERIC BEHNKE, B.S.,1 DAVID PEGUES, M.D.,2 AND ANTONIO A. F. DE SALLES, M.D., PH.D.1

1Department of Neurosurgery, and 2Division of Infectious Diseases, Department of Medicine, David Geffen School of Medicine, University of California Los Angeles, California
Complete resection of the enhancing tumor evaluated by early post-operative MR, 48-72hrs:

Imaging is an independent and overwhelming prognostic factor in patients with newly diagnosed Gliomas.
Surgery – Maximal Resection

Surgery has drawn the most attention as a treatment of gliomas because surgical adjunctive methods including:

- Fluorescence visualization of the tumor by 5-aminolevulinic acid
- Navigation-guided fence-post-procedure
- Intraoperative neurophysiological monitoring (Awake)
- **Intraoperative magnetic resonance (MR) imaging**

Have enabled more extensive resection of gliomas.
Current treatment of low grade astrocytoma: a review.

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Through a comprehensive review of the current literature, the present article investigates several aspects of low grade astrocytomas (LGA), including prognostic factors, treatment strategies and follow-up regimes. LGA are in general relatively slow-growing primary brain tumours, but they have a very heterogeneous clinical behaviour. Several factors affect prognosis, and these include age, histological subtype, and Karnofsky Performance Score (KPS) prior to surgery. Furthermore, a number of different molecular genetic alterations have been shown to affect both the prognosis as well as the course of disease. The current literature seems to support the idea that treatment with radical tumour resection, where possible, yields better long term outcome for patients with LGA. However, decisions about the timing of adjuvant therapy need to be individualised.

Maximal Resection and withold Radiation for time of Recurrence resected LGA yields a longer period of progression-free survival, whereas patients with radically resected tumours should receive radiotherapy at the time of progression. Regarding chemotherapy, we found evidence to suggest that patients respond to both temozolomide (TMZ) and the combination of Procarbazine, Lomustin and Vincristine (PCV) better than Temozolamide. PET scans helps with detection and differenciation between Tumor Progression and Radiation Necrosis.
Conformal Techniques

Multiple Shots to Conform

Shaped Beam Static Single Shot

Shaped Beam Dynamic Single Shot

Less Efficient

Most Efficient Planning Delivery

Hours

Minutes

Intensity Modulation Radiosurgery or SRT

Rapid Arc

Hybrid Arc
Cell Type

Neuronal Activation

Seizures
Glucose Utilization

Demyelination
Breakdown of BBB
Edema

Neuronal Death

Obliteration
Ischemia

Vascular

Early

Glial - Endothelial

Edema

Final

Acute

Evolution

Time course is dose dependent

Months

Necrotic lesion

Late

Early

Delayed
SRT for Low Grade Astrocytoma

5040 cGy / 90%
SRT - Low Grade Oligodendroglioma Cyst Recurrence

2003

2005

5040 cGy / 85%

Speech
SRT for Optic Glioma

Vision

L. ICA


TUMOR
SRT for Optic Glioma

PreSRT

10 beams, 4860 cGy, 90%

Recurrence

3 mo followup
SRT for Pediatric Gliomas

6 y/o intermediate grade glioma

5040 cGy, 90%, 11 beams

4 month followup
UCLA Preferred Approach

- Tumor Board
- Wait for Symptoms – Controlled Seizures
- Surgery – Maximal Resection
- SRT or Conformal Radiation Therapy
- SRS – Unique cases
- Recurrence: Reoperation
  - SRT (if not previous boost)
  - SRS (selected cases)
  - Salvage Chemotherapy
Conservative Management of Presumed Low-Grade Gliomas in the Asymptomatic Pediatric Population

Zarina S. Ali, Shih-Shan Lang, Leslie N. Sutton

Key words
- Conservative
- Incidentaloma
- Low-grade gliomas
- Nonsurgical
- Pediatric brain tumors

Abbreviations and Acronyms
LG6: Low-grade glioma
MRI: Magnetic resonance imaging
MRS: Magnetic resonance spectroscopy
NAA: N-acetylaspartic acid

OBJECTIVE: The optimal management of asymptomatic children with small, nonenhancing intracranial lesions presumed to be low-grade gliomas (LG6s) is not entirely clear in the literature. However, surgical intervention via resection or biopsy is not without risk and is of questionable long-term benefit in children with stable lesions. We present a series of 12 patients with incidentally detected, small, nonenhancing, intracranial lesions that were managed with watchful waiting and serial magnetic resonance imaging (MRI) scans.

METHODS: We retrospectively reviewed a series of 12 children (eight boys, four girls) with T1 hypointense and T2 hyperintense intracranial lesions <2 cm without enhancement or surrounding edema.

RESULTS: Most patients (n = 5, 41.7%) received MRI studies after suffering a traumatic injury with evidence of an abnormality seen on computed tomography scan. Others received MRI scan as part of headache work-up (n = 4, 33.3%). The majority of lesions were located infratentorially (n = 8, 66.7%), whereas other locations included the frontal lobe and thalamus. The median age of the patients upon identification of the intracranial abnormality was 10 years (range, 1–19 years of age). Patients were followed for a median of 16.7 months (range, 2.7–59.5 months). The most common diagnosis based on clinical and radiographic features of these lesions consisted of LG6. No patient underwent surgery, radiation therapy, or chemotherapy except one patient, in whom the lesion grew in size. Surgical pathologic diagnosis in this case confirmed World Health Organization grade II astrocytoma.

CONCLUSIONS: Our case series suggests that conservative management and close follow-up of incidental radiographic lesions consistent with LG6s is a safe and effective initial strategy in the pediatric population. In cases in which lesion size or quality changes, surgical resection may be necessary to confirm diagnosis. Further studies that include a larger number of patients and longer follow-up period are required to compare outcomes between this approach and initial surgical, radiation, or chemotherapy management strategies.
Low-grade gliomas (LGGs) are a diverse group of primary brain tumors that often arise in young, otherwise healthy patients and generally have an indolent course with longer-term survival in comparison with high-grade gliomas. Treatment options include observation, surgery, radiation, chemotherapy, or a combined approach, and management is individualized based on tumor location, histology, molecular profile, and patient characteristics. Moreover, in this type of brain tumor with a relatively good prognosis and prolonged survival, the potential benefits of treatment must be carefully weighed against potential treatment-related risks. We review in this article current management strategies for LGG, including surgery, radiotherapy, and chemotherapy. In addition, the importance of profiling the genetic and molecular properties of LGGs in the development of targeted anticancer therapies is also reviewed. Finally, given the prevalence of these tumors in otherwise healthy young patients, the impact of treatment on neurocognitive function and quality of life is also evaluated.
Markers to Delineate Prognosis and Need for Treatment

Analysis of IDH mutation, 1p/19q deletion, and PTEN loss delineates prognosis in clinical low-grade diffuse gliomas

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These authors contributed equally to this work.

Background. Grades II and III gliomas have unpredictable rates of progression, making management decisions difficult. Currently, several clinical and radiological characteristics are utilized to predict progression and survival but collectively are suboptimal.

Methods. In this study, we analyzed a set of 108 nonenhancing hemispheric grade II–III gliomas. Demographic variables, including patient age, tumor diameter, extent of resection, and performance status, were combined with molecular data (IDH mutation status (mIDH), 1p/19q codetation, PTEN deletion, and EGFR amplification). A complete dataset for all variables was compiled for 70 of the 108 patients. Both univariable and multivariable analyses were performed to determine whether the molecular data singly or in combination offer advantages over tumor type and grade for prediction of overall survival (OS) and/or progression-free rate (PFR).

Results. Patient age, clinical variables (tumor diameter, extent of resection, performance status), and pathology (tumor type and grade) were not predictive of OS or PFR. IDH mutation status alone was predictive of longer OS and PFR for the entire group of tumors; 1p/19q deletion alone was predictive of OS but not PFR. In the multivariable analysis, none of the clinical or demographic factors were predictive of OS or PFR. IDH mutation status, 1p/19q codetation, and PTEN deletion were predictive of OS (P < .003, P = .005, P = .02, respectively). Both mIDH (P < .001) and the interaction term of 1p/19q and PTEN (P < .001) were found to be predictive of PFR.

Conclusions. We conclude that the combination of mIDH, 1p/19q codetation, and PTEN deletion may be particularly effective in discriminating good prognosis from poor prognosis hemispheric gliomas. We propose that such a scheme merits testing on larger prospective cohorts. Should our findings be confirmed, routine clinical analysis of hemispheric gliomas for mIDH, 1p/19q codetation, and PTEN deletion would be justified.
Review

Current treatment of low grade astrocytoma: A review

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ABSTRACT

Through a comprehensive review of the current literature, the present article investigates several aspects of low grade astrocytomas (LGA), including prognostic factors, treatment strategies and follow-up regimes. LGA are in general relatively slow-growing primary brain tumours, but they have a very heterogeneous clinical behaviour. Several factors affect prognosis, and these include age, histological subtype, and Karnofsky Performance Score (KPS) prior to surgery. Furthermore, a number of different molecular genetic alterations have been shown to affect both the prognosis as well as the course of disease. The current literature seems to support the idea that treatment with radical tumour resection, where possible, yields better long term outcome for patients with LGA. However, adjuvant therapy is often necessary. Administering early postoperative radiotherapy to patients with partially resected LGA yields a longer progression free survival compared to surgery alone. If the surgery is incomplete, adding adjuvant chemotherapy to the radiotherapy at the time of progression. Regarding chemotherapy, we found evidence to suggest that patients respond to both temozolomide (TMZ) and the combination of procarbazine, lomustine and vincristine (PCV). However, the response rates in patients receiving PCV seem superior to those of patients receiving TMZ. In follow-up PET scans, the tracers 18F-FDG and MET provide high sensitivities for detection of new suspicious lesions and these tracers are furthermore effective in discriminating between tumour progression and radiation necrosis. The research into biomarkers is currently limited with regards to their applications in LGA diagnostics, and therefore further studies including larger patient populations are needed.
Low-grade glioma (LGG) comprises nearly 20% of all central nervous system glial tumors, with approximately 2000-3000 patients diagnosed annually in the United States. Because of their infiltrative ability and aggressive nature, the average 10-year survival is 30% when <90% of the tumor is resected. Since the 1970s, prognosis for LGGs has improved significantly. This improvement is primarily attributable to earlier diagnoses via magnetic resonance imaging scanning, increased awareness of the more favorable oligo component, technical advances in intraoperative neurosurgery, and stratification for young age. Using a number of prognostic factors, LGGs have been classified into low-risk and high-risk subgroups. Optimal therapy for patients with low-risk, supratentorial grade II glioma remains a highly controversial issue in the neuro-oncology community. The concerns regarding the toxicity of therapy often outweigh the benefits of delaying tumor progression. The recommendation for observation is made without full prospective understanding of the impact of radiologic tumor progression on the quality of life (QOL), neurocognitive function (NCF), seizure control, and functional status of these patients. We present a review of the current knowledge of the management of LGG with emphasis upon patient-reported outcomes of QOL, NCF, and seizure control. We also discuss current clinical trials with proposals to evaluate QOL, NCF, and seizure control in patients undergoing observation alone after newly diagnosed low-risk LGG or treatment options for those patients in the high-risk group.
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<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Surgery: early and gross tumor resection</td>
<td>Risks of surgery (eloquent areas, deep thalamus) when patient is &lt;40 years, has no evidence of radiographic tumor growth, and symptoms are well-controlled (65)</td>
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<tr>
<td>Decreases patient symptoms related to mass effect or intracranial hypertension (65)</td>
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<td>Increases median survival duration (35, 70)</td>
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<td>Decreases incidence of recurrence, time to tumor progression, and incidence of malignant transformation and improves OS and PFS (4, 22, 53, 70, 78, 80, 91)</td>
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<td>Long-term improvement in verbal memory (7, 30, 85)</td>
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<td>Improves seizure control (27, 69, 79, 80)</td>
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<td>Beneficial use of intraoperative mapping and awake surgery to preserve NCF and QOL (17, 18, 21)</td>
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<td>Clinical value of intraoperative confocal microscopy to visualize cellular 5-ALA–induced tumor fluorescence (72)</td>
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<td>Table 2. Management of LGGs</td>
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<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
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<td>Radiation: early and low-dose</td>
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<tr>
<td>- Improves FFS (37, 80, 86, 91)</td>
<td>- Long-term radiation-induced toxicities (dementia, radiation necrosis) (40, 58)</td>
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<td>- Improves OS (77)</td>
<td>- Negatively impacts NCF and QOL (increased fatigue) in the long-term (≥ 12 years) (15, 19, 29, 31, 41, 43, 49, 58, 75)</td>
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<td>- No impairment in NCF and QOL in the short-term (≤ 6 years) (45, 85)</td>
<td>- Delays radiation for patients &lt;40 years, well-controlled symptoms, no evidence of radiographic progression (5, 58, 77, 86)</td>
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<td>- Low-dose radiation has a less likely risk of lower levels of functioning and increased symptom burden compared with high-dose (39, 45, 76, 80)</td>
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<td>- Reduces the incidence of seizures (68, 69, 79, 86)</td>
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<td>Chemotherapy: early</td>
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<td>- Improves NCF, QOL, seizure control (3)</td>
<td>- Discontinuation of TMZ in the absence of progression results in resumed growth within 1 year in 60% of LGG patients, suggesting TMZ treatment should be continued for longer periods of time (67)</td>
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<td>- Upfront chemotherapy may replace radiation with its potential neurotoxicities (80)</td>
<td>- PCV is associated with greater toxicity (myelosuppression) than TMZ (38)</td>
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<td>- Increases response rate and duration of response with associated 1p/19q codeletion (20, 36, 80) and MGMT promoter methylation (20, 28, 48)</td>
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<td>- Decreases the frequency of seizures (20)</td>
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<td>- Upfront TMZ improves QOL (6, 20, 50)</td>
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<td>- Upfront PCV has a prolonged and positive ongoing response after chemotherapy (63)</td>
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OS, overall survival; NCF, neurocognitive function; QOL, quality of life; 5-ALA, 5-aminolevulinic acid; TMZ, temozolomide; LGG, low-grade glioma; MGMT, O6-methylguanine-DNA methyltransferase.
Conclusions

• Patients Expect Intact Function
• “Planned Resection and Complementary Stereotactic Radiation can meet patient’s expectations”
• Stereotactic Radiation may improve tumor control and decrease side effects.

Association of Therapies Guided by Biomarkers
Radiocirurgia da Coluna, Cérebro
Obrigado