Oncofunctional Optimization: Integrated Multimodal Use of Second Window Indocyanine Green (SWIG) Fluorescence, Neuronavigation, Electrophysiological Stimulation, and White Matter Tractography (DTI) in 78 Consecutive Brain Tumor Patients

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Disclosures

I DO NOT have any financial or organizational relationships with commercial interests or other entities. I hereby certify that to the best of my knowledge, no aspect of my current personal or professional circumstances places me in the position of having a conflict of interest with my duties, responsibilities and exercise of independent judgement as an Officer, Member of the Board of Directors, Nominee for Office, Educational Presenter and/or a representative of AANS/NREF/NPA.
Introduction

- “Oncofunctional balance” is a paradigm for neurosurgical oncology in the pursuit of a maximal safe resection
- To optimize and quantify this paradigm, we developed a metric, the Oncofunctional Score (OFS), calculated as the sum total of extent of resection (EOR) and Karnofsky Performance Status (KPS)
- We hypothesized that we could optimize the oncofunctional balance by aiming for ≥80% EOR while maintaining KPS 80 integrating four distinct surgical modalities -- effectively aiming for OFS ≥160
Methods

• We selectively integrated four operative adjuncts in a series of 78 consecutive brain tumor surgeries:
  1. Neuronavigation
  2. White Matter Tractography (DTI)
  3. Second Window Indocyanine Green (SWIG) fluorescence
  4. Cortical/subcortical electrical stimulation in eloquent brain

• OFS = Σ (EOR + KPS) ≥ 160; KPS calculated at first post-op visit

• Retrospective chart review and statistical analyses were performed
Results

OVERVIEW:

• Cohort demographics were tabulated and a sub-cohort of glioma patients was identified
• 72% of patients had improved or unchanged post-op KPS
• Mean EOR for glioma was 89%
• SWIG (ICG Fluorescence) showed 90% sensitivity for high grade glioma (HGG)
• Mean OFS for glioma was 168 with 72% of functional (pre-operative KPS≥80) HGG patients achieving the target OFS of 160
• OFS ≥160 correlated with decreased length of stay (LOS)

Consort Diagram of Glioma Sub-Cohort

Enrollment
78 craniotomy patients consecutively enrolled
Exclusion Criteria: Pregnant woman; iodide allergy

Allocation
Allocation to treatment modalities
• SWIG (n=78)
• Neuronavigation (n=78)
• DTI (n=49)
• Neuromonitoring (n=16)

Surgery/Follow-Up

Analysis
Included in analysis: Glioma (n=55)
• High Grade Glioma (n=50)
• Low Grade Glioma (n=5)
Results

72% (23/32) of functional HGG patients achieved the target OFS≥160

Oncofunctional Score in High Grade Glioma, pre-op KPS ≥80 (N=32)
Results

Higher OFS is a function of increased EOR and superior KPS, and is linked to decreased length of stay.

Statistical Analyses of Glioma Sub-Cohort

<table>
<thead>
<tr>
<th>Univariable analysis of OFS with outcomes</th>
<th>Multivariable regression of length of stay (in days)</th>
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<tbody>
<tr>
<td>OFS (days)</td>
<td>Length of stay, days Coef. 95% CI P</td>
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<tr>
<td>≥160 (n=31)</td>
<td>OFS -0.07 -0.10 -0.03 &lt;0.01</td>
</tr>
<tr>
<td>&lt;160 (n=24)</td>
<td>Gender (ref. female) 0.25 -1.52 -2.03 0.78</td>
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<tr>
<td></td>
<td>Age -0.01 -0.08 -0.06 0.83</td>
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<tr>
<td></td>
<td>Preop KPS (ref. ≥80) -1.49 -4.06 -1.08 0.25</td>
</tr>
<tr>
<td></td>
<td>Preop tumor volume -0.01 -0.04 -0.02 0.71</td>
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<tr>
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<td>Eloquent involvement -0.21 -2.92 -2.51 0.88</td>
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<thead>
<tr>
<th>Postop KPS ≥80 (%)</th>
<th>Logistic multivariable regression of postoperative KPS ≥ 80.</th>
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<tbody>
<tr>
<td>dKPS</td>
<td>Postop KPS (≥80) Odds Ratio 95% CI P</td>
</tr>
<tr>
<td>-2</td>
<td>OFS 1.05 1.01 -1.10 0.02</td>
</tr>
<tr>
<td>-9</td>
<td>Gender (ref. female) 0.81 0.18 -3.65 0.78</td>
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<td>Age 0.95 0.88 -1.02 0.16</td>
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<td></td>
<td>Preop KPS (ref. ≥80) 2.65 0.35 -19.7 0.34</td>
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<td></td>
<td>Eloquent involvement 0.44 0.03 -6.39 0.55</td>
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</tbody>
</table>
Results

A representative HGG patient demonstrates the multimodality approach to maximizing OFS

A 62-year-old woman, pre-op KPS 80, presented with glioblastoma of the dominant frontotemporal lobe (A), as seen with tractography illustrating the adjacent arcuate fasciculus (green), inferior fronto-occipital fasciculi (yellow), and language activation areas from functional MRI (purple) (B). She underwent intraoperative cortical stimulation (C) which, along with SWIG (D), aided in defining the appropriate surgical approach. Following resection, residual SWIG tumor fluorescence was seen linearly along the tumor bed (E) and left by design due to its proximity to the M3 branches of the MCA. This linear enhancement was re-demonstrated on post-operative MRI (F), which showed a near-total resection of 98%. Post-op KPS 70. OFS was 168.
Discussion

- We propose the OFS as a simple but novel metric to quantify maximal safe resection that merits further investigation.

- Literature review shows benefits of EOR>80% in glioma outcomes [1,2]; functional independence (KPS≥80) is also an important measure of successful glioma surgery [3] -- therefore we propose a target OFS of 160.

- Achieving “80/80” EOR/KPS is possible using a multimodality approach, and OFS ≥160 is correlated with improved surgical outcomes in this cohort.

- Further validation of OFS and the 160 target is recommended in prospective studies.


Summary

• Oncofunctional Score (OFS) is a new metric to quantify maximal safe resection and optimize the oncofunctional balance in glioma surgery
• OFS ≥160 is linked to metrics of surgical outcomes (EOR, KPS, length of stay)
• OFS has the potential to be an overall outcomes measurement for glioma surgery, prioritizing resection and functional status individualized to each patient
• Further validation is necessary