Title

SURG-02. A NOVEL RISK MODEL TO DEFINE THE RELATIVE BENEFIT OF MAXIMAL EXTENT OF RESECTION WITHIN PROGNOSTIC GROUPS IN NEWLY DIAGNOSED GLIOBLASTOMA

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prognosis in glioblastoma patients. Functionally, *Qki* and UFA loss both decrease endolysosome-mediated receptor degradation, thereby enriching receptors on the cytoplasmic membrane (e.g., Frizzled and Notch1) that are essential for maintaining stemness. This enrichment of receptor signaling enables GSCs to cope with the low ligand levels outside their niches. On the other hand, lower lysosomal activity induced by *Qki* and/or UFA loss also lead to defective mitophagy, which consequently leads to accumulation of damaged mitochondria, high level of ROS, and genomic instability in Qki-deficient NSCs. We identified that genomic instability induced by *Qki* deletion led to copy number gains of classical glioblastoma-associated oncogenes such as of PDGFRa and Cyclin D1/D3. Lastly, the heterogeneity of *Nestin-CreERT2;QPP* tumors also lead to heterogeneous responses to immunocheckpoint blockade inhibitors including anti-CTLA4 and anti-PD1. Taken together, our data suggest that Qki/UFA loss-induced endolysosomal defects promotes gliomagenesis through both reducing receptor degradation and inducing genomic instability.

SURGICAL THERAPY

SURG-01. AN INTRAOPERATIVE RAMAN SPECTROSCOPIC PROBE FOR GLIOMA SURGERY: INDICATIONS, SAFETY, AND FUTURE DIRECTIONS

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INTRODUCTION: Raman spectroscopy is a tool that utilizes a non-contact label-free modality of optical imaging that measures inelastic scattered photon shifts to give a unique biochemical signature. There is established work showing that these unique fingerprints can differentiate a glioma from necrosis and normal brain. The ability to instantly characterize these organic tissues intraoperatively, then, can help guide a surgeon's resection. The goal of the present study is to review the Raman work that has been performed to date, its demonstrated safety in a rat model and the indications for use of this operative tool. METHODS: We review the fundamental principles of Raman spectroscopy, some contemporary data, and show its effectiveness as an intraoperative probe. Because the probe uses a 100mW 785nM laser wavelength, we also determined the threshold at which it causes damage to cortical grey matter in a rat model. RESULTS: Raman spectroscopy has a high sensitivity and specificity (>97%) when discriminating between grey matter, necrosis and GBM. A discriminant function analysis, supervised classification algorithm, is used for spectral identification to allow relevant spectral interpretation and allows for tailoring to which Raman peaks are significant for diagnosis. In regards to safety, animal experiments showed no damage seen at 10 seconds/250mW and estimated damage to occur at 60 seconds/250mW. We also present an intraoperative workflow of how this tool could be used in the operating room. CONCLUSION: A Raman spectrographic probe is a safe and powerful tool that can provide live intraoperative diagnosis and identify tissue margins. Further work is being done to identify clinical outcomes, the unique fingerprints of other pathological tissues and further differentiate gliomas based on molecular markers like IDH-1.

SURG-02. A NOVEL RISK MODEL TO DEFINE THE RELATIVE BENEFIT OF MAXIMAL EXTENT OF RESECTION WITHIN PROGNOSTIC GROUPS IN NEWLY DIAGNOSED GLIOBLASTOMA

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Although the overall prognostic significance of maximal surgical resection of contrast-enhancing tumor in glioblastoma patients is well established, prior studies have not evaluated the combined importance of resection, molecular markers, patient characteristics, and chemoradiation. Incorporation of these factors may redefine the relative benefit of cytoreductive surgery and establish differing thresholds for extent of resection in varying clinical presentations. In the first study of its kind, we examine the interactive effects of volumetric extent of resection with molecular and clinical factors to develop a new roadmap for cytoreductive surgery. Based on a 20-year retrospective cohort of 850 glioblastoma patients who had initial surgery at UCSF, we employed survival models and recursive partitioning (RPA) to investigate multivariate relationships of overall survival (OS), both in the entire cohort as well as a subset diagnosed since 2005 (Stupp-era) with IDH1 mutation status available (n=470). For the entire cohort and the Stupp-era subset, the RPAs elucidate the combinatorial consequence of treatment, age, IDH1 status (in the subset), and resection of both enhancing and non-enhancing tumor. In the Stupp-era, temozolomide-treated patients that are IDH-wildtype and >65 clearly benefit from a reduction of the enhancing tumor (median OS: 10.1 vs 15.8 months). IDH-wildtype, temozolomide-treated patients under 65 benefit from reduction of both enhancing and non-enhancing tumor with a median survival similar to that of IDH-mutant, temozolomide-treated patients (combined median OS: 33.7 months). The patients faring worst are those that did not receive temozolomide that are >65 and/or have ≥0.3 cm^3 residual enhancing tumor (median OS: 4 months). These risk models outperform all published prognostic models. This is the first study to combine resection of contrast-enhancing and non-enhancing tumor in conjunction with molecular and clinical information in a large single-institution study, and paves the way for rethinking surgical strategies for individual patients with newly diagnosed glioblastoma.

SURG-03. A COMPARISON OF SURVIVAL OUTCOMES AFTER BIOPSY VERSUS RESECTION IN PRIMARY CNS LYMPHOMA: A SINGLE INSTITUTION EXPERIENCE

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INTRODUCTION: Primary CNS lymphoma (PCNSL) is an aggressive, often multifocal neoplasm sensitive to chemoradiation. Surgery has conventionally been diagnostic biopsy rather than resection. Recently, studies have challenged this paradigm, suggesting resection is safe and possibly more efficacious. We addressed this via analysis of our institutions experience. METHODS: A retrospective review was conducted in patients treated with surgery and chemotherapy with or without radiation for PCNSL between March 2002 and February 2018. Indications for surgery were predominantly for tissue diagnosis. Statistical analyses included Kaplan-Meier, log-rank, and Pearsons chi-squared analyses. RESULTS: There were 138 patients (mean age, 61.2-years; range, 14.9–89.7). 5 had GTR, 13 had STR, and 120 had biopsy. Biopsied patients (45/75, 37.5%) harbored more multifocal lesions than GTR (0/5, 0%) and STR (2/11, 15.4%) (p=0.03). Complete remission rates at 6-months were similar in biopsy (67/120, 55.8%) vs GTR (2/5, 40%) or STR (7/13, 53.8%) (p=0.78), even when GTR and STR were combined (p=0.64). There were no differences in PFS between GTR and STR: 8.5-months [95%-CI: 0.2–16.9] vs 21.3-months [4.6–38.0], respectively (p=0.22) or OS: 37.8-months [0–100.1] vs 28.3-months [10.7–45.8], respectively (p=0.96). For biopsy, PFS: 26.5-months [19.9–33.1] and OS: 39-months [30.8–47.2] did not differ from GTR (PFS: p=0.14, OS: p=0.87) or STR (PFS: p=0.83, OS: p=0.30) (Fig. 1). Likewise, when data from GTR and STR were combined (PFS: 17.7-months [0–38.1)], OS: 30.9-months [10.6–51.3]), there remained no significant differences compared to biopsy (PFS: p=0.43) (OS: p=0.50). 7/11 resected patients (6 STR, 1 GTR) had improvement in preoperative deficits after resection, including one with rapid relief of life-threatening mass effect. CONCLUSION: Our experience supports the current surgical paradigm towards PCNSL, demonstrating resection does not improve survival outcomes over biopsy. Resection, regardless of GTR or STR, may have a role in rapid relief of preoperative symptoms, but further studies are needed to answer this question.

SURG-04. SURVIVAL BENEFIT ASSOCIATED WITH GROSS TOTAL RESECTION IN GRADE II ASTROCYTOMAS: AN INTEGRATED ANALYSIS OF THE SEER AND TCGA DATABASE

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