# P.042

## Raloxifene sensitizes glioblastoma cells to hypoxia-induced death through inhibition of stress granule dissolution

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**Background:** Glioblastoma (GBM) is the most common primary malignant brain tumour. Despite aggressive therapy, median survival is only 14 months. Death typically results from treatment failure and local recurrence. The GBM microenvironment is highly hypoxic, which correlates with treatment resistance. Cytoplasmic RNA stress granules (SGs) form in response to hypoxic stress and act as sights of mRNA triage, allowing preferential translation of pro-survival mRNA during stress. We hypothesize that SGs may play a role in hypoxia-induced resistance to therapy, and may be targetable by chemotherapeutics to improve outcomes. **Methods:** We screened 1280 approved compounds to identify drugs that inhibited formation or dissolution of SGs in U251 glioma cells. Raloxifene inhibited SG dissolution in a dose dependent manner. We treated cells with raloxifene and incubated them in hypoxia, and then measured rates of cell death using cell counting and Presto blue. **Results:** Cell death rates were synergistically higher in cells treated with the combination of raloxifene and hypoxia compared to either treatment alone. **Conclusions:** Raloxifene inhibits the dissolution of SGs in glioma cells, and combination treatment results in synergistic tumour cell death. Taken together, this provides evidence that inhibition of SG dissolution may be a viable target for future GBM chemotherapeutics.

# P.043

## Volumetric analysis of low-grade glioma growth in serially-imaged patients

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**Background:** Diffuse low-grade gliomas (LGGs) are infiltrative, slow-growing primary brain tumors that remain relatively asymptomatic for long periods of time before progressing to aggressive high-grade gliomas. **Methods:** We retrospectively identified LGG patients that were stably managed by observation with numerous ($\geq$ 8) serial magnetic resonance imaging (MRI) studies. Tumour volumes were measured by manual segmentation on imaging to study the growth of the lesion. Patient demographic information, tumour characteristics, and histological data were collected from electronic medical records. **Results:** Of 74 LGG patients, 10 (13.5%) patients were included in the study. The number of MRIs acquired ranged from 8 to 18 (median, 11) over a median of 79.7 months (range, 39.8-113.8 months). Tumor diameter increased at a median rate of 2.17 mm/year in a linear trajectory. Cox regression analysis revealed that initial tumour volume predicted time to clinical intervention, and Mann-Whitney *U* test found that patients diagnosed prior to age 50 had significantly slower-growing tumors. Clinical intervention was more likely for tumours larger than 73.8 mL. **Conclusions:** We retrospectively analyzed the natural history of LGGs in patients with numerous serial MRIs managed at a single institution. Comparisons to the literature suggest that this is a subset of particularly slow-growing and low-risk tumours.

# P.044

## Salvage therapy in recurrent pediatric medulloblastoma: A single centre experience

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**Background:** Children diagnosed with medulloblastoma (MB) that are refractory to upfront therapy or experience recurrence have very poor prognoses. Reports of phase I and II studies for these children exist, but bear significant treatment related morbidity and mortality. **Methods:** A retrospective review of children diagnosed with a pediatric MB from 2002-2015 from the McMaster Pediatric Brain Tumour Study Group (PBTSG) captured a number of pediatric recurrent MB. **Results:** Over the 13-year period, 31 children with a histological diagnosis of MB were treated. At two years, 21 (67.7%) of 31 patients were free of recurrence and 25 (80.6%) survived. Thirteen children had recurrent or treatment refractory MB. mean time to recurrence was 14.6 months. The mean follow-up for survivors of recurrent MB was 4.0 years. In 3 recurrent MB, the disease had significantly progressed and the patients palliated. For the remaining children, therapy offered included surgery, radiation, and chemotherapy agents either in isolation or in varying combinations. **Conclusions:** Recurrent MB in our cohort carried a poor prognosis despite administration of salvage therapy. Though there is standardization of the upfront treatment exists, we observed great heterogeneity in the treatment of our 13 patients experiencing recurrence. A greater understanding of the biology of recurrent MB has the potential to guide salvage therapy.

# P.046

## Flow cytometry in cerebrospinal fluid: utility in the diagnosis of central nervous system lymphoma

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**Background:** Flow cytometry in the cerebrospinal fluid (CSF) is used as an adjunct to cytology to increase the sensitivity of detecting central nervous system (CNS) lymphoma. We aim to evaluate CSF flow cytometry as a diagnostic tool for lymphoma in patients presenting with undifferentiated neurologic symptoms. **Methods:** We retrospectively reviewed all CSF flow cytometry samples sent in the Calgary region from 2012-2015. Clinical data, laboratory investigations, radiologic imaging studies, and pathological data were analyzed. Clinical review extended to 2 years post CSF flow cytometric testing. **Results:** The number of samples of CSF flow cytometry that were positive for a hematological malignancy was 43/763 (5.6%). The overall sensitivity of the test was 72.9%. A positive result was more likely to occur in patients with a prior history of a hematological

malignancy or abnormal enhancement on MRI (p<0.0001). In fact, CSF flow cytometry was negative in all patients who did not have a previous hematological malignancy or abnormal enhancement on MRI (n = 247). **Conclusions:** CSF flow cytometry has very limited role in the screening for primary CNS lymphoma, unless a strictly endorsed testing algorithm is applied. It is, however, an invaluable tool in assessing CNS involvement in patients with previous diagnosis of hematolymphoid malignancy.

# P.047

## IDH mutations are associated with pro-inflammatory microglia and macrophages in heterogeneously infiltrated glioblastomas

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**Background:** CNS innate immune cells, microglia and macrophages (MMs), are the largest component of the inflammatory infiltrate in glioblastoma (GBM). They initially participate in tumor surveillance, but are co-opted by GBM to further angiogenesis and invasion. There are no effective immunotherapies against GBM in part because GBM-associated MMs are not well understood. We hypothesized that the extent and inflammatory phenotype of MM infiltration into GBM is variable between patients. This variability could have important implications on immunotherapy selection and treatment outcomes. **Methods:** Using automated quantitation of fluorescently labeled human GBMs, flow cytometry/live cell sorting, collection of conditioned GBM-associated MM media, and corroboration with TCGA and previously published scRNA-seq data, we have uncovered there is surprisingly marked variation in the amount of MM infiltration between tumors. **Results:** MM infiltration can range from almost non-existent, to comprising ~70% of GBM cells. By detecting cell surface markers and secreted cytokines, we determined that a mixture of pro- and anti-inflammatory MMs are found in each tumor. The overall inflammatory phenotype did not depend on the amount of infiltration. Interestingly, IDH-mutant GBM-associated MMs are more pro-inflammatory and less heterogeneous than IDH-wildtype GBMs. **Conclusions:** Taken together, the highly variable immunologic status of GBMs suggests the success of immunotherapies hinges on selecting appropriately vulnerable tumors.

# P.048

## Correlation of preoperative serum lactate, MR spectroscopy and frozen tissue lactate levels as a biomarker for giomas – a prospective clinical study

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**Background:** Lactate, a by-product of glycolysis, has been well established as a marker of poor tissue perfusion. Elevated lactate production is observed in tumor glycolysis known as the Warburg effect. We have previously shown that serum lactate correlated with brain tumor grade. In this prospective study we aimed to determine if the preoperative serum lactate correlated with preoperative MR spectroscopy and in lactate levels in the fresh frozen tissue samples. **Methods:** Twenty-one glioma patients (13 male, 8 female) ages 34 – 86 underwent craniotomy at a single institution by lead author. Tumor pathology revealed a Glioblastoma (n=16), grade II (oligodendroglioma n=1) and Grade III Glioma (anaplastic astrocytoma n=4). Preoperative spectroscopy was performed on 18 patients. A fellowship trained neuro-radiologist (JPC) was blinded to the serum and tissue lactate levels and graded the spectroscopy lactate levels as low or elevated. **Results:** There was direct correlation of spectroscopy tissue lactate levels with serum lactate levels. Pre-operative serum lactate (range 6.6- 29.9 mg/dl) was directly correlated with the fresh frozen tissue lactate levels (range 0.1 – 0.39 ug/mg; Pearson r=0.6 p = 0.0021). **Conclusions:** This study supports that serum lactate correlates with spectroscopy and tissue lactate levels.

# P.049

## Repeat surgery in recurrent glioblastoma: a systematic review and meta-analysis

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**Background:** Recurrent glioblastoma portends a poor prognosis and the role of repeat surgery in improving survival remains uncertain. Our systematic review and meta-analysis aims to address whether re-resection provides a meaningful survival benefit and to what degree. **Methods:** Articles were collected from Pubmed, CINAHL, EMBASE, Medline and Cochrane from January 1990 to 2018. Studies in the temozolomide era with both single surgery and re-resection cohorts were included. Primary outcomes were odds ratio for survival at 6, 12, and 24 months following re-resection and initial surgery. **Results:** Fourteen articles were included for analysis (3048 patients). Meta-analysis showed improved overall survival following re-resection at 6- (OR 1.73, 95% CI 1.23-2.45, p<0.05), 12- (OR 1.71, 95% CI 1.20-2.45, p<0.05), and 24-months (OR 2.24, 95% CI 1.01-4.95, p<0.05). Overall survival from diagnosis or first surgery was also improved in patients who underwent re-resection at recurrence, similarly at 6- (OR 8.22, 95% CI 5.23-12.93, p<0.01), 12- (OR 4.16, 95% CI 3.25-5.36, p<0.01), and 24- (2.35, 95% CI 1.77-3.11, p<0.05) months. Subgroup analyses were done for patients stratified by age, performance status, and number of re-resections. **Conclusions:** Repeat surgery for recurrent glioblastoma is associated with a significant survival advantage independent of other salvage therapies that include chemotherapy, radiation, and other antineoplastic regimens.

# P.050

## NICO-assisted neuroendoscopic management of enlarging subependymal giant cell astrocytoma in tuberous sclerosis complex: a case report

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**Background:** Tuberous sclerosis complex (TSC) is an autosomal dominant neurocutaneous syndrome classically associated with mental disability, seizure disorder and adenoma sebaceum, among other anomalies. One of the major causes of mortality and