is currently a dearth of meningioma-specific QOL tools in the literature. OBJECTIVE: In this systematic review, we analyze the prevailing themes and propose toward building a meningioma-specific QOL assessment tool. METHODS: A systematic search was conducted, and only original studies based on adult patients were considered. QOL tools used in the various studies were analyzed for identification of prevailing themes in the qualitative analysis. The quality of the studies was also assessed. RESULTS: Sixteen articles met all inclusion criteria. Fifteen different QOL assessment tools assessed social and physical functioning, psychological, and emotional well-being. Patient perceptions and support networks had a major impact on QOL scores. Surgery negatively affected social functioning in younger patients, while radiation therapy had a variable impact. Any intervention appeared to have a greater negative impact on physical functioning compared to observation. CONCLUSION: Younger patients with meningiomas appear to be more vulnerable within social and physical functioning domains. All of these findings must be interpreted with great caution due to great clinical heterogeneity, limited generalizability, and risk of bias. For meningioma patients, the ideal QOL questionnaire would present outcomes that can be easily measured, presented, and compared across studies. Existing scales can be the foundation upon which a comprehensive, standard, and simple meningioma-specific survey can be prospectively developed and validated.

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Perceived versus quantified growth trajectory of serially-imaged low-grade gliomas

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Background. Diffuse low-grade gliomas (LGGs) are infiltrative, slow-growing primary brain tumours that remain relatively asymptomatic for long periods of time before transforming into aggressive high-grade gliomas. Surveillance of tumour stability is performed primarily by serial imaging. Methods. We retrospectively identified LGG patients that were managed by observation with numerous (≥ 8) serial magnetic resonance imaging (MRI) studies. Tumour volumes were measured by manual segmentation on imaging. Demographic information, tumour histopathological data, and radiological interpretations were collected from electronic medical records. MRI radiology reports of tumour volume stability were classified into "growth" and "no growth" interpretations. Results. Of 74 LGG patients, 10 (13.5%) patients were included in the study. A median of 11 MRIs (range, 8-18) over a median of 79.7 months (range, 39.8-113.8 months) were analyzed per patient. Tumour diameter linearly increased at a median rate of 2.17 mm/year. Cox regression analysis showed that initial tumour volume predicted time to clinical intervention, and Mann-Whitney U test found that tumours of patients diagnosed before age 50 grew more slowly. Radiology interpretations that reported "no growth" (n=66) corresponded to a median measured growth of 3.90 mL and 11.0% compared to the comparison scan. Reports of "growth" (n=36) corresponded to median measured volume increases of 9.36 mL and 20.5%. Conclusion. We retrospectively analyzed the natural history of LGGs in serially-imaged patients at a single institution. Comparisons to the literature suggest that this is a subset of particularly slow-growing and low-risk tumours. We also highlight the clinical value of performing accurate LGG volumetric analyses.

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A population-based study of melanoma brain metastasis treatment: Has new progress in systemic therapy and new technology in radiotherapy improved patient outcomes?

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Background: Outcomes for patients with melanoma brain metastases (MBM) have been poor. New radiotherapy technologies and systemic agents have improved outcomes. Outcomes have rarely been studied at the population-level. We undertook a population-based study investigating changes in management and outcome for patients with MBM in Ontario from 2007-2016. Methods: This was a retrospective population-based cohort study of patients treated for MBM in Ontario from 2007-2016. Melanoma was identified through the Ontario Cancer Registry. Treatments and outcome were described by era (2007-2009, 2010-2012, 2013-2016). Treatment with cranial radiotherapy and drugs were defined using Cancer Care Ontario data and supplemented by physician billing and drug reimbursement data. Neurosurgery was identified using CIHI hospital records. Time to event was investigated using Kaplan-Meier curves. Results: From January 2007-June 2016, 1096 patients with MBM were treated. Whole brain radiation therapy was the first brain-directed treatment in 75.5% of patients in 2007-2009, dropping to 52.0% for 2013-2016. Patients receiving stereotactic radiation or other conformal techniques as the first brain treatment increased from 3.4% in 2007-2009 to 21.3% 2013-2016. Use of BRAF/MEK inhibitors and immunotherapy increased: <2.0% in 2007-2009 to 40.9% 2013-2016. One-year and two-year overall survival (OS) following first brain-directed treatment was greater in 2013-2016: 21.8% at one year and 13.8% after two years (Wilcoxon p=0.001). This compared to 12.3% and 6.4% 2007-2009, and 10.7% and 5.5% 2010-2012. Conclusion: The advent of new radiation technologies and systemic treatments for MBM was associated with increased survival and greater avoidance of whole brain radiotherapy.

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Is hypofractionation safer than single-fraction radio surgery? The effect of fractionation on radionecrosis

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Introduction: Radiation-induced brain necrosis (RN) is a relatively uncommon (5-20%) but potentially severe adverse effect of stereotactic radiosurgery (SRS) for brain metastasis(BM). We attempted to establish the effect of hypo-fractionation on RN rates by reviewing patients having simultaneous multi-fraction and single fraction treatment of BM at our centre. Methods: Patients receiving simultaneous 1 (20-24Gy) or 3 fraction (21-24Gy) SRS treatments were identified in our institution‟s database. Serial post-SRS MRIs were reviewed to determine the lesion quotient (LQ), or maximum cross sectional area on T1 plus gadolinium divided by

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T2 FLAIR sequences. LQ less than 0.3 was considered RN. Result: Twenty-two patients were followed for a median 320 days. Sixteen patients developed radionecrosis in 21 of 62 lesions (33%), four of which were symptomatic (20%). Eleven of these lesions received 3 fractions and ten received one fraction. RN risk increased with increasing tumor volume (log odds ratio=1.12, p=0.04). There was no difference in incidence of RN in patients who received whole brain radiotherapy (WBRT) (p=0.11), hypo-fractionation (p=0.98) or had a higher maximum dose (p=0.71). Radiographic RN, however, did not clear in any patients who developed it. Eight patients developed a local recurrence (12%), six of which occurred in the single fraction group. Conclusion: Radionecrosis was significantly related to tumor volume but not fractionation, WBRT, or maximum dose. Overall, our results indicate patients receiving SRS for multiple brain metastasis have a higher rate of radionecrosis than the literature and poorer survival despite having equivalent local control.

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Extent of resection in glioblastoma: Incorporating clinical and molecular data

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Background: The benefits of increasing extent of resection (EOR) for both overall survival and progression-free survival (PFS) in glioblastoma has been well documented. However, models predicting surgical outcomes have failed to incorporate a patient"s IDH status, a known prognostic factor. We isolate the impact of IDH on surgical outcomes. We determine the effect modification of increasing EOR and decreasing residual tumor volume (RTV) on IDH status. Methods: We performed a retrospective cohort study of 98 patients with glioblastoma who had undergone either biopsy or surgical resection. Tumor volumes were determined by volumetric analysis. Univariable and multivariable Cox PH Regression models were built using overall survival and PFS as endpoints. Results: Increasing EOR and decreasing RTV were both associated with prolonged overall survival and PFS. When IDH status was added to multivariable models, the model utilizing RTV provided a slightly better fit compared to EOR. An interaction term between RTV and IDH status was characterized, such that at low RTVs the prognosis of an IDH mutant is significantly better than that of an IDH wild-type, an effect that is less important as RTV increases. The significance of this term was confirmed by improved fit upon insertion into multivariable models. Conclusion: Minimizing RTV and increasing EOR are important prognostic factors for both IDH wild-type and IDH mutant glioblastoma. The protective benefit of the IDH mutation at lower RTVs suggests these patients are the best candidates for aggressive surgical resection.

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The impact of repeated surgery on survival for patients with recurrent glioblastoma

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Background: Recurrent glioblastoma portends a poor prognosis and the role of repeat surgery in improving survival remains uncertain. Therefore, we undertook a systematic review and meta-analysis in order to determine if repeat surgical resection provides a meaningful survival benefit for patients with recurrent glioblastoma. Methods: Two independent reviewers searched for articles that reported on overall-survival of patients with recurrent glioblastoma using MEDLINE, Embase, Google Scholar, and Cochrane from January 2000 to 2018. Studies that compared overall survival of patients treated with single surgery compared to repeat surgery in the temozolomide era were included for analysis.Primary outcomes were odds ratio for survival at 6, 12, and 24 months from date of initial diagnosis. Secondary outcomes were ratio odds ratio for survival at 6, 12, and 24 months from date of repeat surgery. The proportions of patients who had the outcomes of interest were pooled using random-effects model. Quality assessment was performed using the Newcastle Ottawa Scale. Heterogeneity across trials was quantified by the I2 statistic. Publication bias was evaluated visually using funnel plots and quantified by the Egger regression. Results: Fourteen articles reporting on 3048 patients were included for analysis. The majority of articles were deemed to be of high quality with Newcastle Ottawa scale greater than 7 points. Pooled analysis showed improved overall survival following repeat surgery 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, $p < 0.05$) and from date of initial diagnosis 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. 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.

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Untangling the NFI-Calpain signaling axis in malignant glioma

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Malignant gliomas (MG) are highly infiltrative tumours with a poor prognosis. Nuclear factor I (NFI) is a family of 4 transcription factors (NFIA, B, C and X) implicated in the regulation of genes involved in MG cell migration and infiltration, particularly the neural stem cell marker, brain fatty acid binding protein (B-FABP). NFI activity is regulated by its phosphorylation status, with hypophosphorylated NFI being the active form. Our results indicate that the phosphatase calcineurin is able to dephosphorylate NFI. In turn, calcineurin is cleaved and activated by calpain proteases. We have identified CAST, a gene that encodes calpain inhibitor, calpastatin, as a putative target of NFI based on chromatin immunoprecipitation. Putative NFI binding elements are located in intron 3 of the CAST gene. To determine whether there is a bona fide alternative promoter within intron 3 of CAST, we carried out gel shifts as well as luciferase reporter gene assays using both the canonical and alternative promoters of CAST. These assays confirmed CAST alternative promoter usage in MG cells. Knockdown of individual NFIs revealed a role for NFIC and NFIX in the repression of CAST gene expression, specifically in cells expressing the hypophosphorylated (active) form of NFI. NFI depletion also altered the subcellular localization of both calpain and calineurin protein. Our results suggest a feedback loop for the

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