Methods: We screened a prospective database of 1892 patients (treated 2006-2017), identified 92 (5%) who lived > 3 years following BM diagnosis, and performed per patient analyses. Results: Median age at diagnosis of BM was 57 years (range 19-77), 77% were women. The most common tumors were lung (50%), breast (26%), thyroid (7%) and skin (5%). 42% had tumors with drug-targetable oncoproteins (e.g. EGFR mutant) and 15% expressed hormonal receptors. ECOG was <2 in 70%. 47% had stage IV disease at diagnosis (75% with brain as the first site). 55% had controlled extracranial disease at the time of BM diagnosis. Median BM diameter was 1.5 cm (range 0.2-7) and 62% had a single lesion. Treatment was with surgery, radiosurgery, whole brain radiation (WBRT), or systemic therapy alone in 38%, 62%, 52%, and 4%, respectively. 53% received targeted- or immuno-therapy. Median follow up was 63 months (range 36-113). 61% failed intracranially at a median 24 months (range 1-99). 5 and 10-year survival (from BM diagnosis) was 82%, and 34%, respectively. Neither upfront WBRT nor other variables tested correlated with improved survival. In patients who died, an MRI was available within 3 months from death in 57%; of those 55% had no active intracranial disease, suggesting that the majority of deaths were non-neurologic. Conclusion: In general, LTS of BM had a limited number of BM, inactive extracranial disease, and drug targetable mutations.

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Radiation induced meningioma in adult survivors of childhood leukemia or primary brain tumor treated with cranial radiotherapy: Incidence and screening recommendations

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Purpose: Cranial radiotherapy (CRT) was commonly given for childhood leukemia and brain tumors. Survivors are at risk of late effects including radiation induced meningioma (RIM). Surveillance for RIM is not standardized . We aimed to determine the incidence, latency, and screening patterns for RIM. Materials and Methods: Retrospective chart review of all patients aged <18 years at the time of radiation (RT), treated with CRT for leukemia or a brain tumor in BC between 1981-2006. Patient, tumor, and treatment characteristics were collected. Actuarial statistics were calculated with Kaplan-Meier Curves. Patients were censored at the date of last normal cranial imaging, or development of a RIM. Results: 392 patients were identified. Median age (range) at CRT was 9.6 years. Median CRT dose was 28Gy. The original diagnosis was leukemia in 50%, glioma in 13%, medulloblastoma in 8%, ependymoma in 7%, neuroectodermal tumor in 7%, germ cell tumor in 5%, craniopharyngioma in 4%, and other pathologies in 6%. Median (range) of clinical follow-up (FU) was 13.2 (0-37.5) years. Median (range) of cranial imaging FU was 15.5 (0-21.2) years. There was no documented cranial imaging FU in 144 patients. Forty-eight patients developed a RIM. The median age (range) at RT for patients with RIM was 6.7 years. Only 8 of these cases presented with associated symptoms. The earliest RIM in our cohort occurred 10.2 years after CRT. On actuarial analysis, the median (95% CI) time to development of a meningioma was 29.8 (28.9-30.7) years. Incidence (95% CI) of meningioma at 10 years was 0%, 15 years was 5 (2-9)%, 20 years was 12 (6-18)%, 25 years was 33 (23-43)% and 30 years was 47 (37-68)%. Amongst patients with a RIM, the median dose of CRT was 45 Gy. The lowest dose of RT in a patient who developed RIM was 12 Gy. RT was delivered to the whole brain in 58% and partial brain in 42% of patients with a RIM. Conclusions: After CRT in pediatric patients, there is a significant risk of developing a RIM and a steady increase in this risk with ongoing follow-up. We recommend standardization of surveillance for these patients with screening beginning 10 years after completion of CRT.

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Characterization of the molecular consequences of CIC-knockout and neomorphic IDH1 R132H mutation on transcriptomic and epigenomic landscapes

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CIC, or Capicua, encodes a transcriptional repressor that is itself repressed by RAS/MAPK signalling. CIC is a recurrent target of somatic mutation in type 1 low grade gliomas (LGG), with at least half of the alterations predicted to be deleterious. Type 1 LGGs are a cohort of tumours that are molecularly defined by the loss of heterozygosity of chromosome arms 1p and 19q and the presence of neomorphic IDH1/2 mutations. Despite the high frequency of mutations in CIC within this tumour type, CIC‟s putative tumour suppressive role remains to be elucidated. It is also unclear how CIC may cooperate with neomorphic IDH1/2 to promote gliomagenesis. To comprehensively characterize the molecular consequences of CIC loss, we performed RNA-seq, Whole Genome Bisulfite Sequencing, and ChIP-seq on 6 different histone modifications on isogenic CIC-wildtype (WT) and CIC-knockout (KO) normal human astrocytes. To also investigate the collective effects of CIC deficiency and neomorphic IDH1 on the transcriptome and epigenome, we generated the same dataset in isogenic CIC-WT and CIC-KO astrocytes possessing the IDH1 R132H mutation. Analysis of differentially expressed genes illustrates the enrichment of oncogenic pathways in specifically the CIC-KO, IDH1-R132H cells, supporting a synergistic relationship between CIC loss and IDH1-R132H in driving tumour progression. Integrative analyses are ongoing to unveil the epigenetic mechanisms underpinning the regulatory changes in these isogenic cell line models.

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A systematic review in quality of life of patients with meningiomas: Effort towards developing a disease-specific questionnaire

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BACKGROUND: Meningiomas are the most common primary benign brain tumors in adults. Given the extended life expectancy of most meningiomas, consideration of quality of life (QOL) is important when selecting the optimal management strategy. There

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