The most commonly mutated genes were; *TP53, CDKN2A/B, KRAS, MYC, RB1, NF1, PIKC3A, STK11,* and *PTEN*. A comparison of GA in our BM cases with unmatched primary tumors from COSMIC revealed differences in the frequency of mutated genes: *TP53* (Lung 85% vs 38%, Breast 63.6% vs 26.0%) *CDKN2A/B* (Lung 33.7% vs 7%, Melanoma 56.2% vs 18%, Kidney 40% vs 2%, UC 34.7% vs 9%), *ERBB2* (Breast 36.3% vs 4%), MYC (Breast 36.36% vs 0.3%), *TERT* (Melanoma 62.5% vs 25%, Kidney 40% vs 2%), *APC* (Colon 100% vs 48%), *KRAS* (Colon 100% vs 31%), *PTEN* (Prostate 50% vs 7%), *TSC1* (Kidney 40% vs 2%), *STK11* (UC 26.0% vs 6%). Our results demonstrate a higher frequency of *TP53* mutations (p=0.001) in metastatic lung cancer, and a higher frequency of *MYC* amplification (p=0.01) in metastatic breast cancer, when compared to primary tumors. The present study demonstrates significant differences in the frequency of mutations between primary tumors and BM. Such differences may play an important role in the pathogenesis of BM and may allow for targeted strategies utilizing existing therapies.

OTHR-07. ESTIMATING INCIDENCE PROPORTION OF BRAIN METASTASES AT DIAGNOSIS AND LIFETIME INCIDENCE AMONG CANCER PATIENTS DIAGNOSED FROM 2010–2015 IN CANADA

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INTRODUCTION: The incidence of brain metastases (BM) among Canadian cancer patients is unknown. We aimed to estimate the incidence proportion (IP) of BM at the time of all cancer diagnoses and during follow-up of cancer patients with the top six primary tumours that are most likely to metastasize to the brain. METHODS: Data on BM at diagnosis from 2010–2015 was obtained from the Canadian Cancer Registry (CCR). Site-specific IPs of BM was estimated for patients from provincial registries that achieved ≥90% complete data. These estimates were applied to the total number of newly diagnosed primary cancers to estimate total number of BM at diagnosis from 2010–2015 in Canada. To estimate the number of lifetime BM that arise from six selected primary cancers including lung, breast, skin melanoma, colorectal, kidney/renal pelvis and esophagus, we applied IP estimates reported in the literature. RESULTS: We identified 1,105,905 cancer cases in the CCR from 2010–2015, of which 519,950 (47%) were from the six primaries. The annual average number of patients with BMs at diagnosis from all cancer sites was approximately 2,800 and was highest for lung cancer(2,400).The site-specific IPs of BM at diagnosis were: lung (9.6%;95% CI: 9.3–10.0%), esophageal (2%;95%CI:1.5–2.7%), kidney/renal pelvis (1.3%;95%CI:1.0–1.5%), skin melanoma (1.1%;95%CI:0.9–1.3%), colorectal (0.3%;95%CI:0.2–0.3%), and breast (0.2%;95%CI:0.2–0.3%).Using clinical and population data from the literature, we estimated that nearly 7,400 lifetime BM cases occur annually for these six primaries. CONCLUSIONS: Each year in Canada, approximately 2,800 BMs from all primary cancers are found at the time of diagnosis and approximately 7,400 lifetime BM occur annually from the six selected primary tumours.

OTHR-08. PREDICTION OF RISK OF CENTRAL NERVOUS SYSTEM METASTASIS FOR AJCC 8TH EDITION STAGE III MELANOMA PATIENTS

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Among common solid tumors, melanoma has the highest risk of CNS metastasis. Improved understanding of the incidence, risk factors, and timing of CNS metastasis is needed to inform surveillance strategies for at-risk patients. Clinical data were extracted from two institutions for AJCC 8th edition stage III melanoma patients, diagnosed from 1998–2014 who had negative baseline CNS imaging within 4 months of diagnosis. The cumulative incidence of CNS metastasis was calculated in the presence of the competing risk of death from stage III presentation, and at benchmark time points 1-, 2-, and 5-years post-diagnosis. The cohort (N=1,918) consisted of patients from major melanoma centers in the US (50.6%) and Australia (49.4%). The first site of distant metastasis was CNS only for 3.9%, CNS and extra-cranial sites (ECS) for 1.9%, and ECS only for 31.2% of patients (N=1918); 15.5% of patients who developed distant metastases (N=708) had CNS involvement at first diagnosis of stage IV disease. Cumulative incidence of CNS metastasis from stage III diagnosis was 3.7% (95% Confidence Interval (CI): 2.9–4.6) at 1-year; 9.6% (95% CI: 8.3–11.0) at 2-years; and 15.9% (95% CI: 14.2–17.7) at 5-years. In multivariable analyses, risk of CNS metastasis was significantly higher for males; younger patients; increasing AJCC stage group; scalp primary tumor site, acral melanoma subtype, and increased primary tumor mitotic rate. Conditional analyses showed that only high primary tumor mitotic rate (>9 per mm2) was significantly associated with risk of subsequent CNS metastasis among patients who survived without CNS recurrence 1-, 2-, and 5-years after the diagnosis of stage III disease. Similar rates of CNS metastasis were observed between these two large, geographically-distinct stage III melanoma patient cohorts. These results provide a framework for developing evidence-based surveillance strategies and for evaluating the impact of contemporary adjuvant therapies on the risk of melanoma CNS metastasis.

OTHR-09. IDENTIFYING EPIGENETIC SIGNATURES IN LUNG ADENOCARCINOMAS THAT PREDICT DEVELOPMENT OF BRAIN METASTASIS

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INTRODUCTION: Metastases are the most common adult brain tumor with half spreading from lung cancers and they reduce median overall survival from 26 to 12 months. There are no robust patient-specific predictors of brain metastasis. Epigenetic signatures predict disease recurrence in other cancers and identifying brain metastasis methylation-based signatures may allow for treatment approaches to high-risk patients that prevent their development. METHODS: In 207 lung adenocarcinomas, multivariate cox time to brain metastasis analyses including clinically-relevant variables (lung tumor size and TNM nodal score) along with significant covariates on univariate analyses were performed. DNA was extracted from 142 of these tumors and profiled on the Illumina Infinium EPIC array. A generalized boosted regression classification model used differentially methylated CpG sites significantly predicting time to brain metastasis in a 70% training cohort cox analysis ($p < 0.05$). Resulting methylation-based risk scores were compared to size and nodal status in a multivariate analysis of the independent 30% testing cohort. RESULTS: Of 207 patients with 72 brain metastatic events, tumor size (HR=1.5, 95%CI 1.1–2.0, p=0.01), N status (N3 vs. N0, HR=9.9, 95%CI 3.1–31, p=0.0001), EGFR status (HR=0.4, 95%CI 0.2–0.8, p=0.014), and age (HR=0.7, 95%CI 0.5–1.0, p=0.039) independently predicted their development. Methylation-based risk scores significantly predicted time to brain metastasis in a univariate analysis of the testing cohort (p=0.03). A multivariate analysis of testing cohort patients identified methylation score as the only independent predictor of brain metastasis (HR=4.3, 95%CI 1.1–17, p=0.038) accounting for tumor size and N score. CONCLUSIONS: Genome-wide DNA methylation signatures predict brain metastasis development in lung adenocarcinomas independent of tumor size and nodal disease. The design of a nomogram combining methylation profile other clinical factors may be used to determine patient specific brain metastasis risk values to guide patient counselling, extent of treatment, and screening.

OTHR-10. THE NATIONAL DISTRIBUTION OF NEWLY-DIAGNOSED BRAIN METASTASES IN ADULTS VARIES WIDELY BY PATIENT DEMOGRAPHICS

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INTRODUCTION: Metastases are oft-cited as comprising approximately half of all adult intracranial neoplasms, and their national composition remains unclear. METHODS: The patient demographics and histologic distribution of newly-diagnosed brain metastasis (BM) patients aged > 18yo without a prior history of cancer (2010–2015) were evaluated using the National Cancer Database, which comprises > 70% of all newly-diagnosed cancers in the U.S. RESULTS: 91,686 adults presented with a newly-diagnosed BM between 2010–2015. The most common sites of brain metastases overall were lung (82% of metastatic cases), breast (4.1%), melanoma (3.2%), kidney (2.9%), and colorectal (1.8%). The overall 1-year and 5-year OS rates for all BMs were 27.0% (95% CI [26.7%-27.3%]) and 5.3% (95% CI [5.1%-5.5%]), respectively. The distribution of primary sites for newly-diagnosed BMs varied by sex, age, and race. Compared to males, more females had BMs from breast (8.4% versus 0.8%) and fewer had BMs from kidney (1.9% versus 3.8%), melanoma (1.9% versus 4.5%), and esophagus (0.3% versus 2.0%). In young adults, particularly those 20-29yo, BMs were more likely from melanoma, genitourinary (in males), and soft tissue than adults in middle and advanced age. Lung carcinomas comprised fewer BMs in Hispanics (66%) compared to Whites (82%), Blacks (83%), and Asian/Pacific Islanders (85%). BMs from kidney and genitourinary primaries were higher in Hispanics (7.3% and 2.4% of BMs, respectively) than in Whites (2.8% and 0.3%, respectively), Blacks (1.8% and 0.1%, respectively), and Asian/Pacific Islanders (2.6% and 0.2%, respectively). Melanoma was more frequent in Whites (3.8% of BMs) and Hispanics (2.5%) compared to Blacks (0.3%) and Asian/Pacific Islanders (0.6%). CONCLUSION: Our results illustrate the national distribution of newly-diagnosed BMs and investigates how the distribution varies by patient demographics.