entire cohort (p=0.016, p=0.035 and 0.034 respectively). A disproportionately high representation of BM detected on the delayed studies was located within posterior circulation territories (compared to predictions based on tissue volume and blood-flow volumes). Conclusion: Considering the safe and potentially high yield nature of delayed MRI sequences, it should supplement the basic MRI sequences in all patients in need of precise delineation of their intracranial disease.

OS2 – 166

doi:10.1017/cjn.2016.333

A Novel Model of Human Lung-to-Brain Metastasis and its Application to the Identification of Essential Metastatic Regulatory Genes

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Brain Metastases (BM) represent a leading cause of cancer mortality. While metastatic lesions contain subclones derived from their primary lesion, their functional characterization has been limited by a paucity of preclinical models accurately recapitulating the stages of metastasis. This work describes the isolation of a unique subset of metastatic stem-like cells from primary human patient samples of BM, termed brain metastasis initiating cells (BMICs). Utilizing these BMICs we have established a novel patient-derived xenograft (PDX) model of BM that recapitulates the entire metastatic cascade, from primary tumor initiation to micro-metastasis and macro-metastasis formation in the brain. We then comprehensively interrogated human BM to identify genetic regulators of BMICs using in vitro and in vivo RNA interference screens, and validated hits using both our novel PDX model as well as primary clinical BM specimens. We identified SPOCK1 and TWIST2 as novel BMIC regulators, where in our model SPOCK1 regulated BMIC self-renewal and tumor initiation, and TWIST2 specifically regulated cell migration from lung to brain. A prospective cohort of primary lung cancer specimens was used to establish that SPOCK1 and TWIST2 were only expressed in patients who ultimately developed BM, thus establishing both clinical and functional utility for these gene products. This work offers the first comprehensive preclinical model of human brain metastasis for further characterization of therapeutic targets, identification of predictive biomarkers, and subsequent prophylactic treatment of patients most likely to develop BM. By blocking this process, metastatic lung cancer would effectively become a localized, more manageable disease.

OS3 – 187

doi:10.1017/cjn.2016.334

Differentiating Radionecrosis from Tumor Progression Using IVIM perfusion Fraction in Brain Metastases Treated with Radiosurgery

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Radiation necrosis occurs in 5-25% of patients who undergo stereotactic radiosurgery (SRS) for brain metastases. Intravoxel incoherent motion (IVIM) uses MRI diffusion-weighted imaging (DWI) to assess regional perfusion. We investigated the utility of IVIM to differentiate recurrent tumor from radionecrosis after SRS. Patients who had SRS and subsequent surgical resection of what was thought to be either tumor progression or necrosis were included. ROIs were contoured on the pre-operative post-Gd T1-weighted images and transferred to DWI images using automated co-registration. The perfusion fraction (f) was calculated using asymptotic fitting and the mean f (fmean), 90th percentile for f (f90), mean ADC (ADCmean) and 10th percentile for ADC (ADC10) were calculated. Pathology reports were used to identify the predominant feature (necrosis versus tumor). Nine patients with ten lesions were included. One lesion exhibited pure necrosis while the other nine were mixed; three were predominantly (>75%) tumor, three predominantly necrosis, and three were equal parts of both. The perfusion fraction was significantly higher in cases with predominantly tumor compared to those with predominantly necrosis (fmean 0.10 ± 0.01 vs 0.08 ± 0.01, p=0.02 and f90 0.22 ± 0.01 vs 0.14 ± 0.02, p<0.001). ADC did not differentiate tumor from necrosis (ADCmean 0.97 ± 0.23 vs 1.02 ± 0.36, p=0.8 and ADC10 0.53 ± 0.29 vs 0.76 ± 0.29, p=0.33). The IVIM perfusion fraction is useful in differentiating recurrent tumor from radionecrosis in brain metastases treated with SRS. This is the first study to evaluate IVIM against the gold standard (histopathology).

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OS4 – 161

doi:10.1017/cjn.2016.335

Activated Wnt Signaling for the Therapeutic Targeting of Treatment-Refractory Medulloblastoma Stem Cells

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Brain tumours represent the leading cause of childhood cancer mortality, of which medulloblastoma (MB) is the most frequent