RADIATION-INDUCED MENINGIOMAS: A PERSPECTIVE FROM THE WEST OF SCOTLAND

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INTRODUCTION: Meningioma is the most common intracranial neoplasm to be induced by ionising radiation. Patients receiving childhood radiotherapy do not have routine surveillance to assess for this delayed complication. We aimed to examine our 30 year cohort of surgically treated meningioma in Glasgow. METHOD: We retrospectively reviewed all patients who underwent surgery for meningioma and identified those who previously had childhood cranial irradiation. We then studied their demographics including gender and age at index cranial irradiation, latency period, histological grade and outcome. RESULTS: In total there were 982 patients with meningioma (WHO Grade 1 – 69%, Grade 2- 26%, and Grade 3- 1%). Of these, 22 patients had a radiation-induced meningioma. Eleven (50%) of these were WHO Grade 1. Median age at diagnosis of meningioma was 38 years old. Most cases were females (15; 68%, and most common indication for childhood irradiation was leukaemia (11; 50%), followed by pineal region tumours (4; 18%). Mean latency from irradiation to meningioma diagnosis was 25 years. Seven (32%) patients had multiple meningiomata; 5 (71.4%) of these had >2 lesions. Eight patients (36%) had recurrent meningiomata. CONCLUSION: Patients receiving cranial radiation should be enrolled into a surveillance program guided by the reported latency period. A local registry of such patients would provide more information on protective and prognostic factors.

USE OF PRE-TREATMENT MRI SCANS TO PREDICT TOXICITY FROM RADIOTHERAPY IN PATIENTS WITH GLIOBLASTOMA (GB)

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Median life expectancy of patients with Glioblastoma (GB) is 24.4 weeks. Current best treatment involves concurrent use of Temozolomide and radiotherapy. However, toxicity from radiotherapy can limit patient benefit. The objective of this study was to determine the ability of pre-treatment MRI scans of the brain to predict radiotoxicity.

This pilot study collected survival and toxicity data from 10 patients aged 65 years or older with a histopathological or radiological diagnosis of GB. Brain MRI scans were used to collect information on tumour characteristics alongside imaging scoring systems to assess medial temporal lobe atrophy, global cortical atrophy and small vessel disease. Scans were analysed by two independent readers.

Median survival for this cohort was 35.2 weeks (range 19–59.3 weeks). The beta correlation scores for total contralateral white matter score, global cortical atrophy and T1 contrast volume and survival were all found to equal 1. Beta-correlation coefficients for microanatomical rating score and Schelten's medial temporal atrophy score were 0.4 and 0.9 respectively. The sum of CTCAE scores for nausea, fatigue and confusion was calculated to provide an overall toxicity score. The mean beta-correlation co-efficient for all scores against toxicity was 1. Use of Bland-Altmann plots showed significant inter-rater reliability for all scores excluding global cortical atrophy. Results from this study suggest a moderate relationship between scan characteristics and increasing toxicity. However, high inter-rater reliability suggests these scoring systems have the potential to be used accurately in clinical practice. A larger study will be conducted to confirm results from this study.

SINGLE CENTRE, RETROSPECTIVE REVIEW OF GAMMA-KNIFE STEREOTACTIC RADIOSURGERY AND OTHER THERAPIES ON PREVALENCE OF SEIZURES IN PATIENTS WITH BRAIN METASTASES

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BACKGROUND: An increasing number of patients with brain metastases (BM) are having stereotactic radiosurgery (SRS), but it is not known whether this causes epilepsy. METHODS: We carried out a retrospective review of patients surviving one-year post gamma-knife SRS at the National Hospital for Neurology and Neurosurgery (NHNN) between February 2012 and April 2017.

Data on seizures during the pre- and post-SRS periods were collected along with information about the primary tumour, metastasis location and previous treatments, including whole brain radiotherapy (WBRT) and surgery. RESULTS: 61 patients were treated with SRS. 6 patients had incomplete records and were excluded. Of the remaining 55, 21 had a seizure at some point. 4 had seizures both pre- and post-SRS, 7 had seizures pre-SRS but not post and 10 patients had de-novo seizures post-SRS. 34 did not have a documented seizure at any point.

Of the 14 patients who had seizures post-SRS, 4 also had both WBRT and surgery, 2 had WBRT and 4 had surgery. 100% (4/4) who had WBRT, surgery and SRS went on to have a seizure. Seizures occurred in 11/25 patients who had previous surgery and 7/11 who had previous WBRT.

The primary tumour and metastasis location had no obvious impact on seizure incidence. CONCLUSIONS: The incidence of new seizures post-SRS is low (18%). Previous surgery and/or WBRT may increase seizure incidence post-SRS. The data is currently being reviewed for effect of tumour/ treatment volume, dose delivered, presence of significant oedema and radionecrosis. A larger prospective study is also underway.

SURVIVAL OF PATIENTS WITH MELANOMA METASTATIC BRAIN METASTASES IN THE ERA OF NOVEL SYSTEMIC THERAPIES IN CARDIFF, WALES

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The incidence of malignant melanoma (MM) is increasing in the UK; it's projected to rise by 7% by 2035. MM has high predisposition to developing brain metastases (BM) with 50–60% of patients being affected. Stereotactic radiosurgery (SRS) and surgery, key interventions in managing patients with BM, have been shown to improve survival outcomes of patients. Patients' prognosis and survival has also significantly improved with the advent of novel therapies in the last few years. It was noted that the Cardiff Neuro-Oncology multidisciplinary team were receiving increasing amount of referrals for consideration of surgery or SRS in patients with MM. 106 MDT referrals were retrospectively reviewed. 31 patients had surgery, 20 patients had SRS and the remaining 54 patients had WBRT. There was no significant difference in the patient distribution. The majority of patients had 1 brain lesion in both groups (in similar proportions). The 12 month survival for the surgical cohort was 65% for immunotherapy group, 55%- targeted therapy and 30%- no therapy. For the SRS group the 12 month survival for immunotherapy was 45%, targeted therapy- 40% and 20%- no therapy. The median OS for surgery versus SRS was 8 and 7 months respectively. The results suggest that simultaneous treatment with surgery or SRS in conjunction with SACT does improve survival. Interpretation of results will have to be taken with caution due to the retrospective nature and the small sample size. Going forward, we will delve deeper and review local progression rates and SACT timing/sequencing in our practice.

THE PREVALENCE OF BRAF MUTATIONS IN PATIENTS WITH GLIOMA: A SYSTEMATIC REVIEW

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BACKGROUND: The V600mutation in the v-raf murine sarcoma oncogene homologue B1 (BRAF) enzyme, is a potential clinically actionable target in gliomas. BRAF inhibitors are in wide clinical use for other tumour types, particularly melanoma. The prevalence of this mutation across all gliomas is not fully elucidated and is needed to inform potential screening and treatment. METHODS: A systematic review using articles on the MEDLINE and EMBASE databases (February 1, 2019) was carried out. A meta-analysis was conducted to calculate the prevalence of BRAF mutations in patients with gliomas across all populations and age groups in a clinical setting. PRELIMINARY RESULTS: The review identified 75 studies including 6316 patients; the ages of participants ranged from 30 days to 90 years with a mean age of 32.75 years. Across all studies, the average prevalence of BRAF mutations was 16% (95% confidence interval (CI) from 12% to 20%) but estimates were highly variable across studies, ranging from 0% to 78%. The average prevalence of BRAF mutations in paediatric group was 15% (95% CI 10% to 20%) while the average prevalence in the adult group was 9% (95% CI 4% to 16%). Low grade gliomas had an average prevalence of 19% (95% CI 14% to 25%) compared with 7% (95% CI 4% to 11%) in high-grade gliomas. CONCLUSIONS: BRAF mutations were found to be more prevalent in pediatric patients and in low grade gliomas. Screening these patients for BRAF mutations and treating them with BRAF inhibitors represents a promising area of future medical practice.

REAL-WORLD EXPERIENCE WITH TEMOZOLOMIDE & SATIVEX IN PATIENTS WITH RECURRENT HIGH GRADE GLIOMAS

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BACKGROUND: Glioblastoma (GBM) is the most common malignant brain tumour in adults with a median survival from progression of 8 months. A recent phase 1 study of temozolomide (TMZ) and 1:1 CBD:THC (Sativex) offers evidence of efficacy in patients with recurrent GBM (NCT01812603). METHODS: All patients receiving TMZ & Sativex (75mg/m^2 daily d1 – 21 q28; Sativex continuously) for relapsed GBM or grade 3 astrocytoma at our centre were identified. Patient, tumor and treatment characteristics were recorded, and response based on sequential MRI scans using modified RANO criteria assessed. RESULTS: 13 patients were treated over 18 months. The median age was 56; 69% were male. All had received initial chemoradiotherapy (12 patients: 60 or 59.4Gy/30–33#; 1 patient: 45Gy/15#). 6 patients underwent reresection at recurrence. 4 patients were treated at first progression, 7 at second progression, and 2 at third or later progression. The median number of cycles of TMZ and sativex was 2. The combination treatment was tolerated well by all patients treated, with no Grade 3 or 4 toxicities, the only complaints being of discomfort in mouth after spray and 'spaced out feeling'. Patients stopped treatment due to evidence of progressive disease on sequential MRI sign or physical deterioration. Median Overall Survival (OS) from initiation was 5.9 months (177 days); Progression Free Surival (PFS) at 3 months was 50%. CONCLUSION: These results highlight some discrepancies in OS in comparison to the previous trial (NCT01812603), but our patients were treated at second/ third recurrence. We agree that the combination is well tolerated.

EXPLORING THE LIVED EXPERIENCE OF A HIGH GRADE GLIOMA

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INTRODUCTION: Brain tumour patients face a variety of challenges during diagnosis and treatment. Although most treating clinicians are familiar with these, it can be difficult to obtain a comprehensive overview of which are the most common problems, which patients they affect and how to address them. METHODS: We conducted a systematic review of all work relating to the lived experience of patients and carers of a glioblastoma. We identified articles published between 2008 and 2018 these had to be published in English, using the search terms cares and patients, lived experience, glioblastoma and perspective with relative alternative terms. We excluded articles that were previous systematic reviews, included low grade/brain metastasis from another primary site and articles that combined results for patients and carers. We extracted key theme and concerns, and summarised and tabulated and developed a discussion/recommendation. RESULTS: We identified 405 potential studies. We rejected 374 after screening abstract and titles, and a further 23 on further review. This left a set of 8 unique publications. The 8 publications included were comprised of qualitative studies that explored patient and carers experience at different points in the patient pathway. The main concerns/themes identified were issues around communication specifically the shock of diagnosis, re-negotiating relationships and finally accessing support. CONCLUSIONS: This is the first systematic review that collates the lived experience of patients with high grade gliomas. It differs from the palliative care literature and from the James Lind Alliance, and is more specific than generic health needs assessments that are being used in practice.

EFFECTIVENESS OF BRAF INHIBITORS IN PATIENTS WITH BRAF V600 MUTATION POSITIVE GLIOMA: A SYSTEMATIC REVIEW

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BACKGROUND: BRAF inhibitor treatment with vemurafenib and dabrafenib have produced significant increases in median overall survival for BRAF V600 mutation-positive melanoma patients and are in wide clinical use. BRAF inhibitors have also been used in an ad hoc fashion in BRAF V600 mutation-positive glioma in a number of glioma subtypes with varying prognoses. METHODS: An electronic search was performed on MEDLINE and Embase on February 1, 2019 to identify studies of any design that reported the outcome of patients with BRAF V600 mutation-positive glioma treated with BRAF inhibitors. Data was collected for demographic information, tumour information (type and grading), BRAF mutation type, prior treatment regimens, type of BRAF inhibitor, dose and duration of treatment, best objective response, progression free survival (PFS), overall survival (OS), glioma specific symptomatic relief and adverse events. PRELIMINARY RESULTS: Seventy-nine case reports, case series and single arm cohort studies with a total of 286 patients were included. Duration of treatment was available for 197 patients and varied from 0.1 to 54 months, with 104 patients still undergoing treatment at the time of publication. Progression occurred in 158 patients (including both low-grade and high-grade glioma) at between 0.805 and 36 months following the start of treatment. 34 people died, at between 0.329 and 40.1 months following the start of treatment. CONCLUSIONS: Our systematic review shows varying clinical effectiveness of BRAF inhibitors in BRAF V600 mutation-positive glioma depending on low-grade or high-grade glioma. This evidence may inform future trials of BRAF inhibitors for glioma patients.

SEMI-AUTOMATED MEDULLOBLASTOMA SEGMENTATION AND INFLUENCE OF MOLECULAR SUBGROUP ON SEGMENTATION QUALITY

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Medulloblastoma is the most common malignant brain tumour in children. Segmenting the tumour itself from the surrounding tissue on MRI scans has shown to be useful for neuro-surgical planning, by allowing a better understanding of the tumour margin with 3D visualisation. However, manual segmentation of medulloblastoma is time consuming, prone to bias and inter-observer discrepancies. Here we propose a semi-automatic patient based segmentation pipeline with little sensitivity to tumour location and minimal user input.

Using SPM12 "Segment" as a base, an additional tissue component describing the medulloblastoma is included in the algorithm. The user is required to define the centre of mass and a single surface point of the tumour, creating an approximate enclosing sphere. The calculated volume is confined to the cerebellum to minimise misclassification of other intracranial structures. This process typically takes 5 minutes from start to finish.

This method was applied to 97 T2-weighted scans of paediatric medulloblastoma (7 WNT, 6 SHH, 17 Gr3, 26 Gr4, 41 unknown subtype); resulting segmented volumes were compared to manual segmentations. An average Dice coefficient of 0.85±0.07 was found, with the Group 4 subtype demonstrating a significantly higher similarity with manual segmentation than other subgroups (0.88±0.04).

When visually assessing the 10 cases with the lowest Dice coefficients, it was found that the misclassification of oedema was the most common source of error. As this method is independent of image contrast, segmentation could be improved by applying it to images that are less sensitive to oedema, such as T1.

FACTORS AFFECTING TREATMENT STRATEGY, COMPLETION OF PLANNED TREATMENT AND SURVIVAL IN OLDER PATIENTS WITH GLIOBLASTOMA

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INTRODUCTION: For older patients with glioblastoma (GBM), age, extent of resection, and performance status are prognostic factors. However, an international survey conducted by our Unit found that >40% of neurosurgeons use age alone to discount surgery in older (65+) patients. The aim of this study was to review management in our Unit for 65+ GBM patients, to inform future approaches. METHODS: Patients 65+ with a new GBM diagnosis in our Unit, between 2014 and 2017, were identified. Demographic data, performance status (PS), comorbidity and frailty indices, together with details of surgical/oncological management and outcome were collected. RESULTS: 78 patients were identified. 78% aged 65–74 underwent maximal safe resection, compared with 45% aged 75–84, and 10% aged 85+. Resection was undertaken in 68% PS1, 73% PS2 and 23% PS3 patients. No PS3 patient completed intended radiotherapy, compared with 79% PS1 and 74% PS2 patients. There was a significant difference in frailty scores of patients who completed scheduled oncological therapy compared with those who did not (median score 2 vs 4.5, p=0.0338).

Median survival was 10 months for patients 65–74, 4 months for aged 75 -84, and 40 days for 85+ (p<0.0167). Median survival was significantly lower for PS3 patients (44 days) compared with PS1 or 2 (9.5 months and 7 months respectively; p<0.0167). CONCLUSION: There is considerable variability in performance status and frailty of 65+ GBM patients. PS3 patients at diagnosis are very unlikely to complete oncological treatment. These factors, rather than age alone, should be used to guide management decisions.

WIRELESS BIOELECTRONICS TOWARDS TREATMENT OF GLIOBLASTOMA MULTIFORME

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