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NCOG-11. FEASIBILITY AND EFFICACY OF AN IPAD-BASED COGNITIVE REHABILITATION PROGRAM IN BRAIN TUMOR PATIENTS

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through 85. Prognosis in these patients is particularly dismal due to more aggressive tumor biology, lower functional reserve and high prevalence of comorbidities. Many studies report cognitive impairment in GBM patients, ranging from 29 to 90%. This study was aimed at evaluating neurocognitive status and comorbidities of an elderly population with high grade glioma and the correlation with clinical and demographical variables. METHODS: Patients underwent an extended neuropsychological evaluation with a battery of standardized tests on 8 cognitive domains: global function (GF); verbal learning (VL); short and long-term memory (STM); executive functions (EF); abstract reasoning (AR); attention (ATT) and visuo-constructional abilities (CA). Moreover, the Cumulative Illness Rating Scale was administered to each patient for comorbidities evaluation. RESULTS: We assessed 69 patients with median age at diagnosis of 74 years (range 65–85). 43 patients (62%) presented multi-domain cognitive impairment, and only 8 (12%) showed no cognitive impairment. Neuropsychological deficit mainly affected executive functions (n=42), short term memory (n=28), long term memory and attention (n=22). Patients with AR deficit had a poorer PFS and OS (p<0.001%). At the follow up, 7 out of 12 patients showed cognitive improvement, 4 resulted furtherly deteriorated and 1 patient was stable. Attention was the most affected function at follow up, while verbal learning was the most improved one. CONCLUSIONS: Our results highlight the high prevalence of cognitive deficits in patients with Glioma. Moreover, this study underlines the need to include cognitive functioning and comorbidities evaluation in the assessment of elderly neuro-oncological patients.

NCOG-08. DETERMINING THE CONTENT VALIDITY OF MEASURES OF BASIC AND INSTRUMENTAL ACTIVITIES OF DAILY LIVING (ADL) IN PATIENTS WITH BRAIN TUMORS: A SYSTEMATIC REVIEW

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BACKGROUND: Brain tumor patients may experience impairments in everyday functioning due to both physical and cognitive symptoms. Measures of everyday functioning may therefore be relevant for brain tumor patients in both clinical trials and practice. Everyday functioning can be assessed using activity of daily living (ADL) outcome measures. There are two categories of ADL: basic activities of daily living (BADL; e.g. washing and dressing) and instrumental activities of daily living (IADL; e.g. shopping or cooking). The aim of this systematic review was to identify outcome measures containing items on BADL and/or IADL that currently are used in studies with brain tumor patients, and to assess the content validity of these instruments. METHODS: Several electronic databases (i.e. PubMed, Embase, Cochrane, PsycINFO and CINAHL) were searched up to April 2017 to identify studies with brain tumor patients that used outcome measures with ADL items. Articles were selected based on predetermined in- and exclusion criteria. RESULTS: The literature search identified 31 unique outcome measures containing items on BADL and/or IADL. There were 22 (71%) outcome measures containing BADL items and 29 (94%) outcome measures containing IADL items. More than half (65%) of the outcome measures contained both BADL and IADL items. The number of BADL items in each questionnaire ranged from 0% to 83%, and from 0% to 100% for IADL items. Only two outcome measures were specifically developed to measure BADL (Barthel Index and Katz-ADL), and two specifically for IADL (Lawton-Brody IADL and preliminary IADL-brain tumor). However, these instruments have not (yet) been validated in brain tumor patients. CONCLUSION: Currently, there is a lack of suitable options to sufficiently measure BADL and/or IADL in brain tumor patients. Validation of currently existing BADL and IADL measures in brain tumor patients seems necessary, or the development of new tools.

NCOG-09. THE LEVEL OF REPORTING OF NEUROCOGNITIVE OUTCOMES IN RANDOMIZED CONTROLLED TRIALS OF BRAIN TUMOR PATIENTS: A SYSTEMATIC REVIEW

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INTRODUCTION: Neurocognitive impairment is frequently present in brain tumor patients and is therefore considered an important outcome in brain tumor research. To use neurocognitive outcomes (NCO) in clinical decision-making, neurocognitive evidence should be of sufficiently high quality. One important aspect in the generation of high quality evidence is the level of reporting. We aimed to investigate the level of neurocognitive functioning reporting in randomized controlled trials (RCTs) in brain tumor patients. METHODS: We conducted a systematic literature search in several databases up to August 2017. Of the selected relevant RCTs, the following data were retrieved: basic trial demographics and NCO characteristics, quality of NCO reporting, and risk of bias. We also analyzed studies that should impact clinical decision-making based on their quality of reporting. RESULTS: We identified 65 RCTs, of which NCO was the primary endpoint in 14 (22%). The included brain tumour types varied, with 20 RCTs studying glioma patients (31%) and 17 studying brain metastatic patients (26%) only. Radiotherapy and chemotherapy were the most studied treatments (both in 31% of studies). In five studies (8%), rehabilitation of neurocognitive impairments was investigated. Important methodological limitations were related to the documentation of statistical approaches for dealing with missing data, and to discussing limitations and generalizability issues uniquely related to the NCO components. Risk of bias was high regarding blinding of personnel and incomplete outcome data. Twenty RCTs (31%), eight with NCO as primary endpoint and 12 as secondary endpoint, satisfied a sufficient number of criteria to be classified as high-quality NCO evidence. Most of these studies did contribute to clinical decision-making. CONCLUSION: Investigators involved in brain tumor research should give attention to methodological challenges related to NCO reporting as identified in this review, as high-quality reporting of NCO evidence can be of value in clinical decision-making.

NCOG-10. EXECUTIVE DYSFUNCTION IN NEUROONCOLOGY: BEHAVIOR RATING INVENTORY OF EXECUTIVE FUNCTION IN ADULT PRIMARY BRAIN TUMOR PATIENTS

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BACKGROUND: Adult primary brain tumor (PBT) survivors report persistent cognitive difficulties throughout treatment which are problematic for everyday functioning, employment capability, and quality of life. Cognitive domains often affected by cancer treatment appear to be attention and executive functioning (EF). One validated measure developed to assess an individual's EF within daily living is the Behavior Rating Inventory of Executive Function – Adult (BRIEF-A). To date, no published research has investigated the EF profile of PBT patients using the BRIEF-A. METHODS: Seventy-four patients from a NCI-designated cancer center completed the BRIEF-A, a validated self-report questionnaire that assesses executive functioning across nine subscales and provides three index scores: Behavioral Regulation, Metacognition, and Global Functioning. Descriptive analyses were conducted to determine the self-reported EF profile in PBT patients. MANOVA's compared the performance of PBT patients to three diagnostic populations (comparison group data obtained from BRIEF-A manual): mild cognitive impairment (MCI), unmedicated attention-deficit/hyperactivity disorder (ADHD-U) and healthy controls (HC). RESULTS: PBT BRIEF-A group means were average across subscales and indexes, yet the prevalence of significant elevations ranged from 12–50%. The Metacognition Index demonstrated a 38% elevation prevalence compared to 22% in Behavioral Regulation. Approximately 61% of the sample had at least one clinically elevated scaled score. When comparing between group profiles, PBT reported significantly more impairment than HC and significantly less than ADHD-U across all subscales. No significant differences were found between PBT and MCI groups. CONCLUSIONS: Despite group means not reaching clinical impairment, a substantial proportion of patients with PBT endorse significant difficulty with executive dysfunction. Elevations were most prominent in metacognitive abilities (e.g., Working Memory), over behavioral dysregulation (e.g., Emotional Control). Notably, the EF profile of PBT patients was remarkably similar to that of MCI, increased when compared to HC, and well below ADHD-U.

NCOG-11. FEASIBILITY AND EFFICACY OF AN IPAD-BASED COGNITIVE REHABILITATION PROGRAM IN BRAIN TUMOR PATIENTS

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OBJECTIVE: To assess feasibility and effect on cognitive function and Health-Related Quality of Life (HRQoL) of an iPad-based intervention in grade 2 and 3 glioma patients stable off treatment. Patients with lower grade glioma suffer significant cognitive dysfunctions that impact their HRQoL. Formal cognitive rehabilitation is a limited resource that may be more available if deployed with a mobile device such as an iPad. METHODS: Stable,

grade 2 and 3 glioma patients with subjective cognitive complaints, complete a baseline computerized battery of standardized cognitive tests using the NIH Toolbox and HRQOL assessment with the FACT-BR. Patients then completed a novel, evidence-based, iPad based, brain tumor specific, cognitive rehabilitation program called ReMind over the next 3 months (~3 hours per week). NIH Toolbox and HRQOL assessments were repeated after completion of the rehabilitation, and again 9 months after baseline. Primary endpoint was feasibility with secondary endpoints of changes in cognitive scores and HRQOL assessments. RESULTS: To date, 10 patients have enrolled and completed baseline testing, of whom 5 have completed ReMind rehabilitation. Median age is 56 years. Median disease duration is 7.6 years. 5 patients have Oligodendrogliomas (IDH mutated and 1p19q deleted), 3 patients have Astrocytomas, IDH mutated, and 2 patients have Astrocytomas NOS. 5 are grade II and 5 are grade III. 5 had left hemisphere tumors, 4 had right hemisphere tumors, and 1 was bilateral. 10 had prior chemotherapy and 8 prior radiation. We anticipate enrolling another 5 – 10 patients and will present the updated feasibility data as well as changes in cognitive and HRQOL scores. CONCLUSION: As patients with lower grade tumors live longer, it is important to increase availability of cognitive interventions to improve HRQOL and outcomes. This iPad based approach provides in-home access to cognitive training and compensation strategies for patients with brain tumors.

NCOG-12. COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) FOR OUTCOME PREDICTION IN ELDERLY PATIENTS (PTS) WITH GLIOBLASTOMA (GBM): A MONO-INSTITUTIONAL EXPERIENCE

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BACKGROUND: Treatment for GBM elderly PTS is still a challenge in neuro-oncology. Clinical tools, including CGA, are needed for improving treatment decision and outcome. The aim of this study was to evaluate CGA as a prognostic tool in terms of PFS and OS in elderly GBM PTS. METHODS: We performed a retrospective analysis of elderly PTS ≥ 65 years, treated at Veneto Institute of Oncology between January 2011 and January 2018, with newly histologically diagnosed GBM and receiving a baseline CGA after 3–4 weeks from surgery. CGA included the following domains: age, activities and instrumental activities of daily living (ADL, IADL), cognitive status (MMSE), mood (GDS), nutritional status (MNA), number of drugs, comorbidity (cumulative Illness Rating Scale-CIRS), presence of geriatric syndromes, presence of caregiver. PTS were classified according to Balducci's criteria into Fit or Unfit (Frail and Vulnerable). RESULTS: 113 PTS were enrolled: 72(64%) were male, KPS were ≥ 70 in 90 PTS(80%); 37 PTS(33%) had a radical surgery, 63% partial surgery and 4% received a biopsy. 90 PTS(80%) received Stupp treatment, 16 (14%) temozolomide or radiotherapy alone and, only 7(6%) received no treatment. MGMT methylation status was analyzed in 96 PTS: 44% were metMGMT. According to CGA evaluation: 40 PTS(35.4%) were classified as Fit and 73 PTS(64.6%) Unfit. PFS was 11.2(95% CI 6.0–16.4) and 7.2(95% CI 5.8–8.6) months for Fit and Unfit PTS (p=0.1). On multivariate analysis, adjusted for type of surgery, MGMT methylation status and type of therapy, PFS was significantly different between the two groups (HR=0.6, 95% CI 0.2–0.9; p=0.04). OS was 16.4(95% CI 14.6–18.2) and 10.6(95% CI 8.3–12.8) ms for Fit and Unfit PTS (p=0.04); on multivariate analysis the HR was 0.51(95% CI 0.2–0.9; p=0.04). CONCLUSIONS: CGA demonstrated significant outcome prediction in terms of OS and PFS, regardless of therapy and it could be a useful treatment decision-tool.

NCOG-13. NEUROCOGNITIVE EVALUATION OF BRAIN METASTASES PATIENTS TREATED WITH POST-RESECTION STEREOTACTIC RADIOSURGERY: A PROSPECTIVE SINGLE ARM CLINICAL TRIAL

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OBJECTIVE: Post-operative radiation therapy for brain metastases (BM) has become standard treatment. Concerns regarding the deleterious cognitive effects of Whole Brain Radiation Therapy (WBRT) spurred a trend to use focal therapies such as stereotactic radiosurgery (SRS). The purpose of this study was to prospectively evaluate the neuropsychological fluctuations that follow post-resection SRS treatment since limited data exist in this context. METHODS: We conducted a prospective single arm cohort study of patients with 1–2 BM, who underwent resection of a single BM

between May 2015 to December 2016. Patients were evaluated for cognitive functions (NeuroTrax test) and quality of life (QOL; QLQ-30, QLQ-BN20) before and 3 months following post-resection SRS. Results: Twelve out of 14 patients completed pre- and post SRS neurocognitive assessments. Overall, we did not detect significant neurocognitive or QOL changes 3 months following SRS. In a subgroup analysis, cognitive changes among patients at the age of 60 or over (n=7) were compared to younger ones (n=5). Both age groups were similar in terms of gender, pre-treatment KPS and ECOG, total SRS treatment volume, lesion eloquence and post-SRS survival. Among patients younger than 60 years, median global cognitive score increased from a pre-treatment score of 88 (72–102) to 95 (79–102), 3 months following SRS treatment, p=0.019; Wilcoxon paired non-parametric test. Immediate verbal memory and executive functions scores increased from 86 (72–98) to 98 (92–112) and 86 (60–101) to 95 (73–108), respectively, p=0.043. No significant cognitive changes were discovered among patients at the age of 60 or older. Conclusion: Post-resection radiosurgery has a safe neuro-cognitive profile and is associated with a relatively preserved quality of life. Patients younger than 60 years benefit more than older ones and may even regain some cognitive functions within a few months after treatment.

NCOG-14. HIPPOCAMPAL N-ACETYLASPARTATE CONCENTRATION CORRELATES TO VERBAL MEMORY BEFORE RADIOTHERAPY FOR BRAIN METASTASES

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BACKGROUND: Changes of quality of life and cognitive function, especially verbal memory, after brain radiotherapy is currently widely discussed in neurooncology with substantial change in the paradigm of treatment of brain metastases. In our previous study, we described the decrease in the hippocampal concentration of N-acetylaspartate (NAA, marker of neuronal density and viability) in response to whole brain radiotherapy (WBRT). The aim of presented analysis is to evaluate the NAA concentration before radiotherapy and to describe the relation to the verbal memory baseline. MATERIAL AND METHODS: Patients with brain metastases indicated to WBRT underwent hippocampal MR spectroscopy (MRS) along with neuropsychological examinations focused among others to verbal memory. Absolute NAA concentrations for right and left hippocampus and the sum of absolute NAA concentrations in both hippocampi were compared with results of AVLT_TR. RESULTS: The examination was performed in 26 patients. Patients were divided into two groups based on median NAA concentration (8.56 mM). The median AVLT_TR was 37 points in the group with hippocampal NAA concentration < 8.56 mM. In the group of patients with baseline NAA concentration ≤ 8.56 mM, the median AVLT_TR was higher with 43 points (Mann-Whitney U Test, p = 0.02). CONCLUSION: Non-invasive examination by hippocampal MRS can predict the baseline pre-radiotherapy cognitive functions, which are normally tested by time-consuming psychological tests. Patients who had lower baseline NAA hippocampal concentrations had a significantly lower baseline verbal memory. NAA hippocampal concentrations may be a useful biomarker for selecting patients who would benefit most from the hippocampal sparing radiotherapy techniques reducing the risk of iatrogenic deterioration of QoL in patients treated with a palliative intent, especially in cases where local brain stereotactic radiotherapy is not applicable or available. Supported by the Ministry of Health of the Czech Republic, grants NV18-03-00469, NV18-03-00398.

NEURO-IMAGING

NIMG-01. A BLINDED IMAGE EVALUATION STUDY TO DETERMINE THE DIAGNOSTIC EFFICACY OF ^{18}F-FLUCICLOVINE PET, AS AN ADJUNCT TO MRI IMAGING, IN ADULTS WITH GLIOMA

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The Response Assessment in Neuro-Oncology (RANO) working group have emphasized the clinical utility of Positron Emission Tomography (PET) imaging in brain tumour, highlighting the superiority of amino acid PET tracers over glucose PET tracers in diagnosis, treatment monitoring, and response assessment (Albert, 2016). The amino acid PET tracer ^{18}F-fluciclo-