

with neurocognitive risks and has modest validation. Recently, the Pediatric Neuro-Oncology Rating of Treatment Intensity (PNORTI) was developed to evaluate the impact of treatment intensity on psychosocial outcomes but has not been compared to neurocognitive outcomes. This study compared the NPS and PNORTI in terms of relationship to neurocognitive outcomes known to be at risk in PBT survivors. **METHODS:** 88 PBT survivors' neuropsychological outcomes were retrospectively analyzed in relation to the NPS and PNORTI. Variables of interest included IQ, working memory, and processing speed. **RESULTS:** NPS associated with lower IQ ( $rs=-.476$ ,  $p=.001$ ), lower working memory ( $rs=-.323$ ,  $p=.010$ ), and lower processing speed ( $rs=-.389$ ,  $p=.007$ ) in patients diagnosed at a younger age, but only processing speed for children diagnosed after age 7 years ( $rs=-.262$ ,  $p=.036$ ). PNORTI was not correlated with neurocognitive variables for either group. **CONCLUSION:** NPS has value in predicting neurocognitive outcomes, though much more in a younger age at diagnosis group compared to older patients. The PNORTI did not demonstrate predictive value for these neurocognitive domains in our sample. Given the potential clinical and research value of a summary rating of treatment burden relating to long-term outcome, future research should include relationship to psychosocial outcomes and quality of life.

#### QOL-12. CLINICAL SIGNIFICANCE OF RADIATION-INDUCED CEREBROVASCULAR DISEASE IN CHILDHOOD BRAIN TUMOR SURVIVORS

Tiina Remes<sup>1,2</sup>, Maria Suo-Palosaari<sup>3</sup>, Niina Ritari<sup>1</sup>, Riina Puosi<sup>1</sup>, Päivi Koskenkorva<sup>4</sup>, Anna Sutela<sup>4</sup>, Sanna-Maria Toivainen-Salo<sup>1</sup>, Pekka Arikoski<sup>4</sup>, Mikko Arola<sup>5</sup>, Emma Hovén<sup>6</sup>, Päivi Lähteenmäki<sup>7</sup>, Tuula Lönnqvist<sup>1</sup>, Pekka Riikonen<sup>4</sup>, Kirsti Sirkkiä<sup>1</sup>, Heikki Rantala<sup>3</sup>, Marika Harila<sup>2</sup>, Marja Ojanieni<sup>2</sup>, and Arja Harila-Saari<sup>8</sup>; <sup>1</sup>Helsinki University Hospital, Helsinki, Finland, <sup>2</sup>Oulu University, Oulu, Finland, <sup>3</sup>Oulu University Hospital, Oulu, Finland, <sup>4</sup>Kuopio University Hospital, Kuopio, Finland, <sup>5</sup>Tampere University Hospital, Tampere, Finland, <sup>6</sup>Karolinska Institutet, Stockholm, Sweden, <sup>7</sup>Turku University Hospital, Turku, Finland, <sup>8</sup>Uppsala University, Uppsala, Sweden

**BACKGROUND:** Childhood brain tumor survivors have a high risk of early cerebrovascular disease, but currently its clinical significance is unknown. **METHODS:** In a nation-wide study, we investigated 68 childhood brain tumor survivors treated with radiotherapy by using magnetic resonance imaging (MRI) and neuropsychological examination after median follow-up time of 20.6 years (range 5.0 – 33.1 years) since radiotherapy. Associations between imaging markers of cerebrovascular disease, white matter hyperintensities and the results of neuropsychological examination were investigated. **RESULTS:** Majority (65 %) of the survivors was diagnosed with cerebrovascular disease at median age of 27.1 years (range 16.2 – 43.8 years). The presence of imaging markers of cerebrovascular disease or white matter hyperintensities was associated with poorer performance in verbal (VIQ) and performance (PIQ) intelligent quotient, working and semantic memory, executive functions, visuospatial ability, and immediate and general auditory memory ( $P < 0.05$ ). Survivors with microbleeds performed worse in PIQ, processing speed, executive functions, and visuospatial ability ( $P < 0.05$ ). Lacunar infarcts were associated with difficulties in visuospatial ability ( $P < 0.05$ ). Survivors with white matter hyperintensities in MRI had higher impairment of working and semantic memory, visuospatial ability, and general auditory memory ( $P < 0.05$ ). Cerebrovascular and small-vessel disease burden associated with poorer neurocognitive performance. **CONCLUSION:** The imaging markers of cerebrovascular disease and white matter hyperintensities were related to poorer cognitive performance in radiation-treated long-term survivors of childhood brain tumor. Longitudinal studies are urgently needed to investigate how cerebrovascular disease and related cognitive impairment progress in the survivors.

#### QOL-13. NEUROCOGNITIVE OUTCOMES ACCORDING TO RISK-ADAPTED TREATMENT REGIMENS FOR CHILDREN OLDER THAN 4 WITH MEDULLOBLASTOMA AND POSTERIOR FOSSA EPENDYMOMA – RESULTS OF THE HIT2000 TRIAL

Martin Mynarek<sup>1</sup>, Anne Neumann-Holbeck<sup>1</sup>, Anika Resch<sup>2</sup>, Holger Ottensmeier<sup>3</sup>, Katja von Hoff<sup>4</sup>, Thomas Traunwieser<sup>5</sup>, Rolf-Dieter Kortmann<sup>6</sup>, Denise Obrecht<sup>1</sup>, Monika Warmuth-Metz<sup>7</sup>, Brigitte Bison<sup>7</sup>, Torsten Pietsch<sup>8</sup>, Stefan M. Pfister<sup>9,10</sup>, Martin Sill<sup>9,11</sup>, Marcel Kool<sup>9,11</sup>, Dominik Sturm<sup>11</sup>, David Jones<sup>11</sup>, Andreas von Deimling<sup>12,13</sup>, Felix Sahn<sup>9,13</sup>, Tanja Tischler<sup>1</sup>, and Stefan Rutkowski<sup>1</sup>; <sup>1</sup>Department of Pediatric Hematology and Oncology, University Medical Center Hamburg Eppendorf, Hamburg, Germany, <sup>2</sup>Department of Pediatrics, University Hospital Rostock, Rostock, Germany, <sup>3</sup>Department of Pediatric Hematology and Oncology, University Children's Hospital Wuerzburg, Wuerzburg, Germany, <sup>4</sup>Department of Pediatric Hematology and Oncology, Charité – University Medicine, Berlin, Germany, <sup>5</sup>Swabian Children's Cancer Center, University Hospital Augsburg, Augsburg, Germany, <sup>6</sup>Department of Radiation Oncology,

University of Leipzig, Leipzig, Germany, <sup>7</sup>Institute of Diagnostic and Interventional Neuroradiology, University Hospital Wuerzburg, Wuerzburg, Germany, <sup>8</sup>Institute of Neuropathology, Brain Tumor Reference Center of the German Society for Neuropathology and Neuroanatomy (DGNN), University of Bonn, DZNE German Center for Neurodegenerative Diseases, Bonn, Germany, <sup>9</sup>Hopp Children's Cancer Center Heidelberg (KITZ), Heidelberg, Germany, <sup>10</sup>Department of Pediatric Hematology and Oncology, Heidelberg University Hospital, Heidelberg, Germany, <sup>11</sup>Division of Pediatric Neurooncology (B062), German Cancer Research Center (DKFZ) and German Cancer Consortium (DKTK), Heidelberg, Germany, <sup>12</sup>Clinical Cooperation Unit Neuropathology (B300), German Cancer Research Center (DKFZ), Heidelberg, Germany, <sup>13</sup>Department of Neuropathology, Heidelberg University Hospital, Heidelberg, Germany

**OBJECTIVES:** Reduced neuropsychological outcomes are a major concern in pediatric patients with malignant brain tumors. We aimed to estimate decline in cognitive function according to treatment regimens. **METHODS:** Cross-sectional analysis of cognitive functions tested with the Neuropsychological Basic Diagnostic tool (NBD) in 279 patients >4 years at diagnosis (median: 8.66; range: 4.01–18.98) with medulloblastoma ( $n=110$ , 23.7–25.0Gy CSI;  $n=131$ , >30Gy CSI) or posterior fossa ependymoma ( $n=38$  local radiotherapy) who participated in the HIT-2000 trial. Multivariable regression analysis was conducted to adjust for postoperative cerebellar mutism syndrome, preoperative hydrocephalus, postoperative shunt placement, the interval between diagnosis and assessment, sex and age. **RESULTS:** Mean time from diagnosis to assessment was 5.1 years. Increasing CSI-dose was significantly associated with a deterioration in performance of most subtests, particularly in areas of fluid intelligence (mean z-values per test for no CSI/23.4Gy/>30Gy respectively: matrix reasoning: -0.40/-0.52/-0.98,  $p<.001$ ), short-term memory (number recall: -0.07/-0.58/-0.64,  $p=.002$ ), visuo-spatial skills (visual-motor integration: -0.49/-0.68/-1.12,  $p<.001$ ) and fine motor skills (dominant-hand: -1.09/-1.80/-2.12,  $p=.008$ ; non-dominant-hand: -1.47/-2.59/-2.82,  $p=.003$ ; bimanual coordination: -1.33/-2.68/-2.76,  $p=.001$ ). These differences were retained after adjustment for confounding variables. Within medulloblastoma patients treated with >30Gy CSI, selective attention, but no other function was reduced in patients treated with pre-radiotherapy chemotherapy including intraventricular MTX (selective attention (with chemotherapy/without chemotherapy mean z-values: -0.66/0.00,  $p=.006$ )). Patients with SHH-activated medulloblastoma did significantly better than WNT or Group3/Group4 medulloblastoma patients in fluid intelligence and fine motor skills. **CONCLUSION:** CSI dose among other highly relevant factors had significant effects on neuropsychological outcome. Pre-radiotherapy intraventricular MTX had only minor effects. Patients with SHH-activated medulloblastomas showed a more favorable outcome when compared to patients in the other subgroups.

#### QOL-14. A BIOPSYCHOSOCIAL APPROACH TO BRAIN INJURY REHABILITATION FOLLOWING TREATMENT FOR PAEDIATRIC BRAIN TUMOURS: CAN PHARMACOTHERAPY AID NEUROPSYCHOLOGICAL OUTCOME?

Jo Phillips and Mark Brougham; Royal Hospital for Sick Children, Edinburgh, Lothian, United Kingdom

Long term survival following paediatric brain tumours has vastly improved in recent decades. Consequently there is a drive towards improved quality of survivorship. Brain tumours, surgical resection and adjuvant therapies represent mechanisms for brain injury and can therefore negatively impact a child's neuropsychological trajectory; affecting cognition, behaviour, emotional and adaptive functioning and educational/occupational outcomes. A biopsychosocial approach to rehabilitation should target each of these domains through supported remediation, environmental modification and psychoeducation for young people and the key systems around them (e.g. families, education). There is a growing evidence base for the role of concordant psychopharmacologies to improve neuropsychological outcome. Since 2015 children treated at RHSC Edinburgh for brain tumours have been offered pharmacotherapy alongside usual rehabilitation approaches if they demonstrate significant difficulties with Attention, Processing Speed and/or Executive Function on formal neuropsychological assessment. Patients are referred to a Consultant Psychiatrist or Paediatrician (as per local protocol) for medication selection, titration and monitoring. A short case series (N=14) is presented outlining brain tumour pathologies, treatment modalities, neuropsychological profile and rationale for recommending pharmacotherapy. Approximately 50% of patients took up the offer. The treatment/s offered and self or parents reported outcomes is summarised. Pharmacotherapy was broadly effective; "it's been like night and day", although for one case (N=1) the side effects outweighed any benefit; "she became even more emotional". Findings indicate that pharmacotherapy should be considered alongside conventional neurorehabilitation techniques for CYP with specific cognitive difficulties following treatment for paediatric brain tumours.