POSTER PRESENTATIONS

P02 RADIOBIOLOGY

P02.01 A STRATEGY TO PERSONALIZE THE USE OF RADIATION IN PATIENTS WITH BRAIN METASTASIS BASED ON S100A9-MEDIATED RESISTANCE

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BACKGROUND: Finding effective treatment options for patients with brain metastasis remains an unmet need. Given the limitations imposed by the blood-brain-barrier for systemic approaches, radiotherapy offers a superior ability to access the brain. While clinical practice recently adapted the use of stereotactic radiosurgery (SRS), Whole-Brain-Radiotherapy (WBRT) continuous to be an important treatment option, since many patients present with multifocal lesions or bad performance scores, rendering them ineligible for SRS. Unfortunately, overall survival of patients remains unaffected by radiotherapy. Despite this clinical data, the molecular mechanisms that allow metastatic cells to resist radiotherapy in the brain is unknown. MATERIAL AND METHODS: We have applied WBRT to experimental brain metastasis from lung and breast adenocarcinoma and validated their resistance *in vivo*. RESULTS: An unbiased search to identify potential mediators of resistance identified the S100A9-RAGE-NFκB-JunB pathway. Targeting this pathway genetically reverts the resistance to radiotherapy and increases therapeutic benefits *in vivo*. In two independent cohorts of brain metastasis from lung and breast adenocarcinoma patients, levels of S100A9 correlate with the response to radiotherapy, offering a novel approach to stratify patients according to their expected benefit. In order to make this biomarker also available for brain metastasis patients receiving palliative WBRT without preceding surgery, we complemented our tumor-specimen based approach with the less invasive detection of S100A9 from liquid biopsies. Here, serum S100A9 also correlated with a worse response to WBRT in brain metastasis patients. Furthermore, we have validated the use of a blood-brain-barrier permeable RAGE inhibitor to restore radio-sensitivity in experimental brain metastasis models *in vivo* and in patient-derived organotypic cultures of radio-resistant brain metastasis *ex vivo*. CONCLUSION: We identified S100A9 as a major mediator of radio-resistance in brain metastasis and offer the molecular framework to personalize radiotherapy by exploiting it as a biomarker and as a therapeutic target, thus maximizing the benefits for the patient.

P02.02 MODELING OF RESPONSE TO IRRADIATION IN RECURRENCE GLIOBLASTOMA'S CELLS CULTURE

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BACKGROUND: Radiosensitivity of glioblastoma (GB) cells of local relapses may be markedly different from the primary tumor. Optimal doses and regimes of re-irradiation GB recurrence is not determined yet. MATERIAL AND METHODS: GO1 primary GB cell culture was obtained during removal of a recurrent tumor after combined treatment, including irradiation of the surgical bed. Cell's culture was irradiated by photon beams with energy 6 MeV and dose rate 600 MU/min. Irradiation performed in 1, 3 and 5 fractions, by 10 different doses for each regime. The dose range was determined experimentally for one fraction (5–250 Gy); for other regimes it was calculated according to the biological equivalent dose conception (3 fractions: 5–450 Gy, 5 fractions: 5–550 Gy). The proliferative activity of cells was investigate by MTT test. The results were normalized to the control. Dose-effect curves were plotted for each irradiation regime. The experimental data were approximated by calculated curves obtained by selecting the optimal parameters of the LQ-model and it's modification. RESULTS: Irradiation of GO1 by 1 fraction with the dose 5–250 Gy, causes a slow decrease in proliferative activity, which reaches a minimum value of 23% at 150 Gy and then remains constant. After irradiation by 3 fractions, proliferative activity of the GO1 gradually decrease only at a total dose over 120 Gy and reaches 37% after 450 Gy. When GO1 was irradiated in 5 fractions, a similar dose-effect curve was obtained, gradual decrease was observed to a value of 52% in the range of 250–500 Gy. Thus, the experimental dose-effect curves for irradiation of recurrence GB cells for 3 and 5 fractions have the appreciable "shoulder", which could be explained by increased radioresistance. When approximating the experimental data by fitting the parameters of the LQ-model, the use of $\alpha/\beta = 8$ provided the slope of the curve, close to the experimental data. For reflecting the "shoulder" an additional summand was introduced into the mathematical expression for the number of proliferating cells - a 105 Gy for 3 fractions and 255 Gy for 5 fractions. CONCLUSION: Modified LQ-model could be used for an adequate mathematical description of the effectiveness of fractionated irradiation in relapsed GB culture cells in vitro. It's necessary to introduce a summand into the formula that determines the formation of a "shoulder" on the dose-effect curve for this. The research was supported financially by RFBR (Project No. 18-29-01061).

P03 COGNITION IN BRAIN TUMORS

P03.04 PRIMARY CNS LYMPHOMA OF THE CORPUS CALLOSUM: PRESENTATION AND NEUROCOGNITIVE PROGNOSIS. STUDY OF A MONOCENTRIC COHORT OF 27 PATIENTS.

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BACKGROUND: The corpus callosum (CC) is frequently involved in primary central nervous system lymphomas (PCNSL). The aim of our study was to describe the impact of these lesions on neurocognition of patients presenting with PCNSL of the CC (PCNSL-CC) and their post-therapeutic evolution. MATERIAL AND METHODS: This is a retrospective single-center study. Patients newly diagnosed at Pitié Salpêtrière Hospital from (1999–2018) were included in this study according to the following criteria: age >18, immunocompetent patient, pathological confirmation (Diffuse Large B cell lymphoma) and CC as main location of the tumor on MRI. Clinical, neuroradiological and neuropsychological data of the patients were collected. In addition, prognostic factors for the neurocognitive outcome of the patients were investigated. RESULTS: 27 patients were included (median age: 67 years, median KPS: 70). At the time of diagnosis, 74% of patients had cognitive impairment and 59% of patients had balance disorders. The cognitive functions most frequently affected were memory and executive functions. Tumor lesions in the CC had a median maximum diameter of 5 cm with a so called "butterfly pattern" in 92% of cases. All patients received a high dose methotrexate based polychemotherapy, including one with radiation therapy, and 67% of patients achieved a complete remission (CR). Median PFS and OS were 33.3 months and 177.9 months respectively. With a median follow-up of 48 months (range 6–156), despite CR, there were still abnormal values in 17% of patients on overall efficiency, 17–55% of patients on executive function tests, 45–55% of patients on memory tests. No significant impaired values were found for visuo-spatial and language tests. Splenial location and age ≥ 60 years were significantly associated with worse episodic memory scores throughout the follow-up. CONCLUSION: PCNSL-CC are associated with frequent cognitive dysfunctions, especially memory impairment, which may recover only partially despite CR, that warrant specific rehabilitation. Older age (≥ 60) and splenial location have worse neurocognition outcome.

P03.05 THE USE OF SUBCORTICAL INTRAOPERATIVE ELECTRICAL STIMULATION MAPPING FOR ASSESSMENT OF EXECUTIVE FUNCTIONS: A SUMMARY OF THE EVIDENCE SO FAR

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BACKGROUND: Over the past years, the functional subcortical architecture of the brain has been increasingly acknowledged in neurosurgical planning. A method to study anatomo-functional correlations is direct electrical stimulation (DES). DES is widely used by neurosurgeons and considered as a reliable tool to minimize the occurrence of permanent postoperative motor,