FDG-PET image analysis were calculated. **RESULTS:** 162 patients underwent SRS+/- WBRT in a 5 year period. During follow-up, 11 patients had surgery-confirmed RDN. There are 11 patients (3 women) with 12 lesions, 3 from a breast cancer, 6 from a lung tumor, 1 from a melanoma, 1 atypical meningioma and 1 glioblastoma. 9 of them were treated with both SRS and WBRT, and the 3 others with WBRT alone. The mean age was 65.36 (range: 44–77) years. The median time between the completion of radiation therapy and the suspicion of RDN was 19.7 (range: 3–34) months. With the evolution, it was observed an evident increase in the size of surronding oedema (2–6 times) by FLAIR RMI. We estimate a PPV 0.40 and NPV 0.80 for perfusion MRI, and PPV 0.25 and NPV 0.75 for FDG-PET, respectively. **CONCLUSION:** The diagnostic performance of both techniques in our series is low and similar to published data; therefore its results must be carefully interpreted in each case. It is peremptory to implement new diagnostic tools in the standard of care with better diagnostic outcomes.

P14.94 MITOCHONDRIAL DNA COPY NUMBER IN NEW ONSET AND RECURRENT GLIOBLASTOMA AND ITS EFFECT ON RADIATION RESISTANCE AND PATIENT SURVIVAL

P. Sravya[1], V. P. Nimbalkar[1], N. N. Kanuri[1], S. Rao[1], A. Arivazhagan[1], S. Somanna[1], P. Kondaiah[2], V. Santosh[1]; [1]National Institute of Mental Health and Neurosciences, Bangalore, India, [2]Indian Institute of Science, Bangalore, India.

BACKGROUND: Recent evidence shows that mitochondrial DNA (mtDNA) content is responsible for radiation resistance in various cancers, but not evaluated in glioblastoma(GBM).Hence,we studied the role of mtDNA content in GBM pathogenesis and treatment response. **MATERIAL AND METHODS:** Archived FFPE tissues of newly diagnosed GBM(n=130), recurrent GBM (n=32 pairs) and non-neoplastic control brain(n=30) with available clinical details were utilized for the study. Immunohistochemistry, Sanger's sequencing, methylation specific PCR and fluorescent in-situ hybridization were used to study IDH, ATRX and TERT promoter mutations, MGMT promoter methylation and EGFR amplification. mtDNA content was analyzed using quantitative real time PCR (relative quantification) and was calculated using the formula $2^{-\Delta\Delta CT}$x100. Malignant glioma cell lines U87 and LN229 were used to study the difference in mtDNA content following radiation exposure.LN229 cell line was subjected to mtDNA depletion by incubation with ethidium bromide for 4 days.The parent and mtDNA depleted LN229 cell lines were then assessed for sensitivity to radiation and Temozolomide(TMZ) therapy using MTT assay. **RESULTS:** mtDNA content was lower than control brain tissue(mean mtDNA content 19.6) in all cases studied,with significantly lower content in older patients(p=0.04).Lower mean mtDNA content was seen in IDH wild type, MGMT unmethylated and EGFR amplified tumors when compared to their counterparts(p=1.06).Survival analysis using Cox regression showed that lower mtDNA copy number is associated with higher risk and hence poorer prognosis(p=0.047).Paired tumor analysis was performed in 32 patients with recurrence of whom only 19 had received radiation therapy (RT).The mean mtDNA content was higher at recurrence as compared to the primary tumor in those who received RT(mean at diagnosis 20.1; mean at recurrence 49.3, p=0.02) while no significant difference was observed in those who did not receive RT. U87 and LN229 cell lines exposed to radiation (0, 2, 4 and 6Gy) showed an increase of 8% and 25% in mtDNA content, respectively, after 6Gy radiation exposure.LN229 parent cells showed a radiation dose dependent decline in cell viability(86% at 2Gy, 68% at 4Gy and 50% at 6Gy).The mtDNA depleted LN229 cells were 100% viable at 0, 2 and 4 Gy and 82% viable at 6Gy.The IC50 of TMZ in parent LN229 cells was 69.3 µM while in the mtDNA depleted cells,it was 100.8 µM. **Conclusion:**Our study shows that lower mtDNA content is associated with poorer survival in GBM.RT increased the mtDNA content in both patient samples and malignant glioma cell lines.mtDNA depleted LN229 lines are more radio-chemo resistant than parent LN229 lines,thus showing that lower mtDNA content leads to treatment resistance.Hence,we establish the significant role of mtDNA content in the pathogenesis and treatment resistance of GBM.

P14.95 IS THE PATHOLOGICAL-GRADE RELEVANT IN "IDH-WILD TYPE, TERT-MUTANT" DIFFUSE-GLIOMAS? AN ANALYSIS IN 147 PATIENTS

A. E. Danyeli, C. B. Akyerli, A. Dinçer, E. Coşgun, U. Abacıoğlu, M. Pamir, K. Özduman; Acibadem Mehmet Ali Aydinlar University, School of Medicine, Istanbul, Turkey.

BACKGROUND: Although the word "glioblastoma" still denotes a grade-IV pathology, basic molecular studies have clearly indicated that a significant proportion of lower-grade gliomas harbor genetic alterations typical of glioblastomas. Based on these findings cIMPACT-NOW update 3 has defined an entity called the "diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV". A TERT-promoter mutation is one of these typical molecular markers of glioblastomas. In this study we analyzed IDH-wild type, TERT-mutant diffuse gliomas of different pathological grades to look for differences in demographic, clinical and survival characteristics. **MATERIAL AND METHODS:** 147 adult hemispheric diffuse-gliomas with wild-type IDH1/2 and mutant TERT-promoter (C228T or C250T) were retrospectively analyzed. Primary thalamic, cerebellar brainstem or spinal cases were excluded. 126 (86%), 16(11%) and 5(3%) patients were WHO grade IV, III and II respectively. After surgical treatment or stereotactic biopsy all patients underwent chemoradiation. Median follow-up was 16mo (1–110). Tumors of different grades were compared for age, gender, multifocality, gliomatosis pattern, Ki-67 index, progression-free survival and overall-survival. **RESULTS:** Mean age at presentation for grade II, III and IV were comparable (58.1, 58 and 58.1; ANOVA, p=0.72). There was a slight male predominance in both lower-grades and WHO-grade IV (M:F ratios 1.625 and 1.74). Mean Ki-67 index was significantly higher in higher grades (0.06, 0.14 and 0.25 for grades II, III and IV; ANOVA, p=0.001). Multifocality was comparable (chi-sq, p=1) in lower-grades (3/21; 14.3%) vs. WHO-grade IV (18/126; 14.3%). Gliomatosis pattern was comparable (chi-sq, p=0.095) in lower-grades (2/21; 9.5%) vs. (3/126; 2.3%). Median recurrence free survival (RFS) was 16 months (0–63) in lower-grades and 8months (1–50) in WHO-grade IV. PFS was significantly different between 3 WHO-grades (Log rank, p=0.007) and also between lower-grades and WHO-grade IV (Log rank, p=0.002). Median overall survival was 26 months(2–110) in lower-grades and 15mo(1–91) in WHO-grade IV. OS was significantly different between 3 WHO-grades (Log rank, p=0.014) and also between lower-grades and WHO-grade IV (Log rank, p=0.007). **CONCLUSION:** Increasing pathological grades of hemispheric "IDH-wild type, TERT-mutant diffuse gliomas" have similar demographic and clinical characteristics but incrasing proliferation indices, decrasing progression free survival and shorter overall survival. The findings may be suggesitve of different grades of one common tumor entity.

P14.96 GLIOMATOSIS CEREBRI IMAGING PATTERN: A TREATMENT-INDEPENDENT MARKER FOR WORSE OVERALL SURVIVAL IN WHO GRADE II AND III GLIOMAS

I. Divé[1,2], E. Steidl[3,2], M. Wagner[3], M. C. Burger[1,2], K. Franz[4], P. N. Harter[5], O. Bähr[1,2], E. Fokas[6], U. Herrlinger[7], J. P. Steinbach[1,2]; [1]Dr. Senckenberg Institute of Neurooncology, Frankfurt am Main, Germany, [2]University Cancer Center Frankfurt (UCT), Frankfurt am Main, Germany, [3]Institute of Neuroradiology, University Hospital Frankfurt, Frankfurt am Main, Germany, [4]Department of Neurosurgery, University Hospital Frankfurt, Frankfurt am Main, Germany, [5]Institute of Neurology (Edinger-Institut), University Hospital Frankfurt, Frankfurt am Main, Germany, [6]Department of Radiooncology, University Hospital Frankfurt, Frankfurt am Main, Germany, [7]Department of Neurology, University Hospital Bonn, Bonn, Germany.

BACKGROUND: The term gliomatosis cerebri (GC) refers to glial brain tumors with widespread tumor expansion affecting three or more cerebral lobes. Formerly considered a distinct tumor entity, recent studies found no difference in the mutational profile of glial tumors with GC growth pattern compared to non-GC gliomas. Thus, in the new WHO classification of brain tumors, GC is no longer included as a separate diagnosis. While the presence of gliomas with GC growth pattern is associated with worse overall survival (OS), the underlying factors remain to be identified. Here, we asked whether differing therapeutic strategies in first line treatment could account for the worse outcome of patients with GC growth pattern and grade II and III histology. **MATERIAL AND METHODS:** From the patient data bank of the University Cancer Center (UCT) Frankfurt, 47 patients with histological diagnosis of WHO grade II or III glioma, and with record of GC imaging pattern were identified. GC tumor expansion was confirmed by review of MRI scans prior to treatment initiation. Patients with WHO grade II or III glioma without GC growth pattern served as control cohort (n=379). IDH mutational status was available for 75% of GC tumors (IDH R132H mutated 32%; non-mutated 43%) and 69% of non-GC tumors (IDH R132H mutated 57%; non-mutated 12%). **RESULTS:** Within the GC patient cohort, patients with tumors without contrast enhancement, lower WHO grade and mutated IDH status showed better OS. Compared to the control cohort, patients with GC had significantly shorter OS. This was independent of histological diagnosis or IDH mutation status. Patients with GC more frequently underwent radiochemotherapy (17% vs. 9% in the non-GC cohort), and drastically more often received chemotherapy alone (51% vs. 5%). We then analyzed OS in GC and non-GC patients that had received the same first line treatments. For radiochemotherapy in GC versus non-GC patients, OS was 1.1 years vs. 12.7 years (p =0.0075, log-rank test). For upfront chemotherapy alone, OS was significantly shorter in the GC cohort than in the non-GC cohort (3,6 years vs. undefined, p =0.0016, log-rank test). **CONCLUSION:** Differences in first-line treatment cannot account for the worse prognosis of patients with GC imaging pattern. Further studies are needed to pinpoint biological or clinical factors that might influence responsiveness to therapy and prognosis of GC tumors.