

11.1 months in INI1 + tumours as compared to 6.5 months in INI1 – tumours. No patients were alive in the un-methylated and INI1 – tumour subgroup.

**Conclusions:** In our series, at the level of protein expression by immunohistochemistry, loss of INI1 in GBM may be indicating an underlying molecular aberration accounting for the more aggressive clinical behaviour.

## Po10-7

### Histological characterization of low-grade diffuse astrocytomas

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Human astrocytomas are well known for their histological diversity. In connection with a retrospective clinico-pathological study on low-grade astrocytomas during the time period 1987–2007, all patients found in the hospital electronic patient data base, were investigated. Paraffin-sections re-examined, and tumours were classified according to the WHO 2007 criteria. All grade II astrocytomas were included ( $n = 96$ ). The aim of the present study was to unveil the multitude of histological features in this type of astrocytoma.

Of special variants we defined approximately 92% as fibrillary, 5% as gemistocytic, and 3% as protoplasmic astrocytomas. In some tumours smaller areas with protoplasmic and gemistocytic appearance were seen. Cell density and cellular/nuclear atypia were predominantly judged to be low to moderate. Occasional mitoses were identified in about 25% of the tumours, and apoptotic figures occurred in about 40%. Microcystic changes, microcalcification, and Rosenthal fibres were seen in 37%, 5%, and 10%, respectively. In about 60% of the cases secondary changes were found, distributed as perineuronal (56%), angiocentric (22%), and subpial growth (16%).

Our findings verify the heterogeneous histology of grade II astrocytomas making this diagnosis often challenging, emphasizing the need to a continuous evaluation of classification systems in conjunction with correlations between histology and survival.

## Po10-8

### HIF-1 $\alpha$ , VEGF, PRL 3 and MMP-9 in Gliomas: an MR correlation

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**Introduction:** Spatial distribution of hypoxia inducible factor 1-alpha (HIF-1 $\alpha$ ), vascular endothelial growth factor (VEGF), phosphatase of regenerating liver-3 (PRL3) and matrix metalloproteinase-9 (MMP9) was compared in progressive grades of glioma and metastatic lesions. MRI parameters relating to hypoxia, invasiveness and angiogenesis were compared with marker expression.

**Materials and Methods:** 65 cases of Glioma including 5 grade-I, 15 grade-II, 4 grade III, 41 grade IV and 5 metastatic tumors. Biopsies were graded and classified by WHO classification (2007), immunostained & percentage tumor cells quantified. Conventional and DCE-MRI with implementation of pharmacokinetic model was for permeability (Ktrans and Kep) calculation and analysis of concentration time curve for hemodynamic indices (CBV and CBF). Institutional ethical approvals were obtained. One way ANOVA was performed for marker expression across groups & Pearson's correlation among perfusion indices and markers

**Results:** Invading tumor cells expressed PRL3, MMP9 and VEGF. HIF-1 $\alpha$  was focal. Endothelial cells expressed VEGF and PRL3 in high grade lesions. In all groups, kep and ktrans showed a posi-

tive correlation with MMP-9 expression, while VEGF correlated with CBV.

**Table 1. IHC parameters in tumors.**

Tumor	PRL3	VEGF	HIF (in hot spots)	MMP9
Glioma Grade 1	52.6 + 32.7	17.2 + 16.8	9.0 + 7.24	30.0 + 21.2
Glioma Grade 2	54.6 + 26.7	16.5 + 10.2	17.7 + 11.3	37.4 + 22.4
Glioma Grade 3	62.5 + 17.0	28.7 + 11.5	28.0 + 8.52	35.0 + 5.47
Glioma Grade 4	61.6 + 28.6	47.2 + 11.3	34.7 + 18.8	48.5 + 19.2
Metastases	88.5 + 9.8	86.5 + 4.6	27.5 + 12.3	72.0 + 6.7

(figures denote mean + SD)

**Conclusion:** MR perfusion parameters correlated with VEGF expression while permeability indices correlated with MMP9.

## Po10-9

### Histological characterization of human glioblastomas

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It is claimed that human glioblastomas (GBM) have a highly variable histologic appearance. In a retrospective clinico-pathological study on primary glioblastomas during the time period 1997–2006, a total number of 193 tumours were included. Available paraffin-sections were re-examined, and multiple histopathological features were recorded.

Most cases were classified as 'classical' GBM (92%), but subtypes like giant cell- and small cell glioblastoma were diagnosed as well (1% and 7%, respectively) Further, a mixture of different types of tumour cells were common including gemistocytes, epitheloid, granular, spindle, small cells, and giant cells. Oligodendroglial components were observed in 5%. Cellularity varied from low to high and atypia from mild to severe. Necroses were observed in almost all cases (99%) and occurred as focal, large, and bland necrosis in 16%, 29%, and 54%, respectively. Mitotic activity varied considerably with a median of 8 (range 0–64) per 10 HPF. Among other findings were: pseudopallisading 83%, microvascular proliferation 83%, apoptotic figures 100%, desmoplasia 42%, nucleoli 49%, and microcalcification 12%. Secondary phenomena observed were subpial- (10%), perineuronal- (24%), and angiocentric growth (19%).

Our findings confirm the histological heterogeneity of this tumour, which is appropriate with its previous name glioblastoma multiforme. For this reason, the diagnosis of this tumour is challenging in such a way that immunohistochemistry and molecular genetic analyses may be required. Nevertheless, the combination of pleomorphic cells, necrosis, and microvascular proliferation strongly favours the diagnosis of a GBM.

## Po10-10

### Immunohistochemical findings of intraparenchymatous metastases of the central nervous system

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Metastatic and secondary neoplasms affect the central nervous system either by bloodborne dissemination from a distant site or by direct local extension. Metastatic neoplasms are common intracranial masses with expansive growth pattern encountered both at sur-

gery and autopsy. Adults are primarily affected. Metastatic carcinoma to the brain usually affects the cerebral hemispheres and/or the cerebellum. To describe the immunohistochemical aspects of intraparenchymatous metastases to the central nervous system, the authors describe 169 cases of metastases evaluated between 1995 and 2008. The brain and the cerebellum were the most common sites of metastases (about 75%), being the lungs (22.36%), the kidneys (16.21%), the breast (14.85%) and the colon (8.1%) the most frequent primary sites. No association was found in relation with the primary neoplasm and the site of metastases ( $P = 0.125$ ). The immunohistochemical analysis was performed in 76 cases, and the expression of the antibodies, in special cytokeratins pattern, was able to suggest the primary site in all cases, making this method a special step to study these lesions.

#### Po10-11

### Histological types of primary central nervous system tumors associated to topography, age, gender and immunohistochemical features

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A major focus of surgical neuropathology has been to associate tumor classification based on histopathologic features to clinical data and immunohistochemical features to determine clinicopathologic entities. Advances in neuroimaging techniques now permit precise tumor localization and accurate sampling of multiple areas within heterogeneous tumors. To describe the histological types of primary central nervous system tumors associated to localization, age, gender and immunohistochemical features, the authors describe 821 cases of primary tumors evaluated between 1995 and 2008. The most common histological types were glioblastoma, diffuse astrocytoma and meningioma (WHO grade 1), with association between tumor localization and age. The immunohistochemical analysis was performed in 48 cases of malignant undifferentiated neoplasias, and the expression of the antibodies was able to suggest the tumor differentiation, making this method a special step to study these lesions.

#### Po10-12

### Differential diagnosis of low grade astrocytoma and reactive gliosis - immunostaining for peripheral benzodiazepine receptors may provide additional tool

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The differential diagnosis of low grade astrocytoma and reactive gliosis can be a challenging problem in surgical neuropathology in the era of stereotactic and navigation-guided biopsies, usually yielding small tissue samples. Numerous criteria for differential diagnosis have been proposed, including Ki67 labeling index, p53 staining, etc. These are not very helpful and demonstrate significant overlap between gliosis and astrocytoma. Peripheral benzodiazepine receptor (PBR) is composed of a multiprotein complex located on the contact site between inner and outer mitochondrial membranes. PBR is found in various peripheral organs and glial cells of the central nervous system. The function of PBR in the glia is not clear, but it has been established that PBR expression is significantly increased in 'activated' reactive astrocytes in neurodegenerative, inflammatory and demyelinating diseases. We proposed that immunohistochemical staining for PBR could be useful in differentiating reactive gliosis from low grade astrocytoma.

Paraffin sections from 35 cases of astrocytoma (WHO grades I and II) and 25 cases of reactive gliosis (caused by brain metastases, cra-

niopharyngiomas, pineocytomas, demyelinating lesions and post-radiation gliosis) were stained for Ki-67, p53 and PBR. Both Ki-67 labeling index and p53 expression demonstrated no significant differences in the cases of gliosis and astrocytomas. However, immunohistochemical staining for PBR demonstrated striking differences in astrocytomas and gliosis. Most astrocytomas showed negative results on PBR staining, while weak focal staining was observed in three cases only.

In all the cases of reactive gliosis, strong to moderate cytoplasmic staining for PBR was seen. This difference was even more striking in cases of gliosis with pilocytic and Rosenthal fibers *vs.* pilocytic astrocytoma and gliosis with gemistocytes *vs.* gemistocytic astrocytoma.

According to our results, immunohistochemical staining for PBR may provide a useful tool for differentiating between low grade astrocytomas and reactive astrogliosis, especially helpful in small samples of tissue.

#### Po10-13

### Diagnostic methods in primary central nervous system lymphomas (PCNSL)

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Primary central nervous system lymphomas, (PCNSL) is now thought to constitute about 0.8–6.6% of all intracranial neoplasms and its occurrence is still growing up. These tumours most commonly arise in the deep cerebral structures including periventricular white matter, corpus callosum, cerebellum, spinal cord. Modern standards of PCNSL diagnosing comprise stereotactic biopsy of the tumour with subsequent histopathological and immunohistochemical differentiation. Diagnosing of malignant small-cell brain tumours may be difficult, especially when only biopsy material is available, but open resection of PCNSL may lead to worse therapeutic effect. The best schema of the treatment is still discussed.

We analysed data of 232 patients subjected to stereotactic biopsy (Brain-Lab system) of deep CNS tumors in last 9 years. Routinely stained smears (Harris hematoxylin& eosin) were prepared for intraoperative cytologic diagnosing. Remaining material underwent histological and immunohistochemical investigations (LCA, CD79alpha and CD20, CD3, CD2, CD4, CD8, CD10, CD15, CD30, ALK1 Protein, Bcl 6, light chains lambda and kappa, pan CK, EMA, Ki67 labelling index). Histological and immunohistochemical investigations enabled us to diagnose 38 PCNSL: 32 B-cell, 3 T-cell, 1 B-cell-T-cell rich and two anaplastic large-cell lymphoma according to WHO (2008) classification. In 24 cases establishing diagnosis on the basis of cytologic smears was difficult, sometimes impossible, because of significant cell necrosis. Cytologic diagnostics of stereotactic biopsies of PCNSL is difficult, because steroids recommended before surgery to prevent herniation, cause necrosis of the tumour. Ultra-small tissue samples obtained by stereotactic biopsy are sufficient to establish a correct diagnosis in PCNSL cases and to implement correct patients treatment.

#### Po10-14

### Development of myofibroblastic sarcoma in meningioma: a new variant of 'metaplastic' meningioma

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Myofibroblastic tumours of meninges are extremely uncommon; only a few cases were previously described, including one with sarcomatous change.