research project as clinical data, imaging features and quality of life evaluation.  

Conclusions: The creation of a formal ontology is the starting point to share and collect data from multiple datasets. It allows to obtain a clear and a common interpretation of concepts, to report information in standardized large database. Along these lines the multi-professional team has in use a suitable support to implement decision support system based on predictive models.

**EP-1354**  
Impact of evaluation timing in determining patterns of failure in glioblastoma  
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**Purpose/Objective:** To determine patterns of failure (POF) and survival outcomes in newly-diagnosed glioblastoma (ND-GBM) patients treated on prospective phase I and II clinical trials using standard chemoradiotherapy in combination with novel chemotherapy.  

**Materials and Methods:** POF of 77 patients with ND-GBM enrolled in prospective clinical trials were reviewed. Patients received the current standard of care, including surgical debulking, conformal radiation therapy (RT), and temozolomide, as well as an investigational chemotherapy agent (everolimus, erlotinib, or vorinostat). Patients received follow-up MR imaging per protocol at 2-month intervals following treatment to evaluate response. Contrast enhancement (CE) from T1-weighted post-contrast MRI scans was used to define each recurrence volume at the time of progression (RecVolp). Additionally, the first suspicious scan containing new or increased CE was used to define the initial recurrence volume (RecVol). MRI scans were registered to the RT planning CT and dose volume histograms were calculated for each RecVol. POF at the time of progression (POFp) and initial indication (POFi) were characterized by the percent volume encompassed within the 95% dose region as central (V 95% ≥ 95%) or non-central (V 95% < 95%). Here, POFp and POFi of each patient were categorized as central only, non-central only, or both central and non-central.  

**Results:** Of the collective patient cohort, POF appeared to become increasingly non-central and multifocal with time. Recurrence with a non-central component increased from 14% to 27% (p = 0.07) and multifocal recurrence increased from 6% to 16% (p = 0.12) from the time of initial indication to progression, respectively. POF depended on the novel chemotherapy agent given. POFi were (94% central, 6% non-central, 0% both) for erlotinib, (79%, 0%, 21%) for everolimus, and (77%, 18%, 5%) for vorinostat patient cohorts. Patients with unmethylated MGMT promoter had a higher percentage of multifocal recurrence (40%) compared to those with methylated MGMT promoter (0%) at the time of progression (p = 0.01). The overall median PFSp, PFSi, and OS were 4.5, 8.6, and 17.4 months, respectively. Survival outcomes based on the novel chemotherapy agent given were not significantly different.  

**Conclusions:** POF for this ND-GBM cohort treated with novel chemotherapy agents were predominantly central, but were influenced by the time point of analysis. POF of the overall cohort were increasingly non-central at progression as compared with initial progression, suggesting that recurrence originates from the central region. POF differed between novel agents despite similar survival outcomes. Robust and properly-timed dosimetric POF analysis may be helpful to evaluate biologic aspects of novel therapeutic agents.

**EP-1355**  
How to low-dose fractionated radiotherapy change outcome in unresectable GBM? Analysis between two schedules  
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**Purpose/Objective:** To compare two schedules of hypofractionated radiochemotherapy in naïve unresectable GBM in terms of toxicity, response and survival: the first one was followed by low dose radiation therapy (Hypo-RT-CT+LDRT), in the second schedule no low dose radiation therapy was administered (Hypo-RT-CT).  

**Materials and Methods:** Patients (KPS > 70, age >18 years) underwent biopsy or with gross residual tumor after surgery were enrolled in these two studies. In the first study (Hypo-RT-CT), patients received hypofractionated radiotherapy (35 Gy in ten fractions) combined with Temozolomide (75 mg/m² from the start to the end of RT); in the second study (Hypo-RT-CT+LDRT) patients received hypofractionated radiotherapy (30 Gy in ten fractions) with concomitant Temozolomide. In both studies adjuvant Temozolomide (5 mg/m²) was administered but it was combined with low dose radiation therapy (40 cGy twice on day for 5 days) only in Hypo-RT-CT+LDRT study. In all cases clinical target volume (CTV) was ring enhancement with residual tumor plus 3 cm. Acute and late toxicities were evaluated according to Common Terminology Criteria for Adverse Events version 4.0. MRI was used in order to evaluate the response to the treatment, according to RECIST Guidelines. Moreover overall survival (OS) and progression-free survival (PFS) were calculated by the Kaplan-Mayer method.  

**Results:** Forty-two patients (M/F: 25/17) were enrolled from June 2010 to May 2014. Twenty-two of 42 patients were enrolled in Hypo-RT-CT while 20 pts in Hypo-RT-CT+LDRT study. Most of them (57%) was submitted only to a biopsy (Table 1). Two out of 22 patients (9%) of Hypo-RT-CT study presented acute toxicities G2 (seizure and headache); in Hypo-RT-CT+LDRT we recorded G2 acute toxicities in 4 patients (18%): 2 thrombocytopenia and 2 leucopenia; G3 acute toxicity was observed only in one patient. After hypofractionated radiochemotherapy, partial response (PR) and stable disease (SD) were of 22% and 40% respectively in Hypo-RT-CT study, 9% and 14% in Hypo-RT-CT+LDRT. Median follow-up was of 24 months (range 6 - 53). Median OS and 1- yrs survival were of 15 months and 75% respectively for Hypo-
RT-CT and 17 months and 67% for Hypo-RT-CT+LDRT (Fig 1). In Hypo-RT-CT and Hypo-RT-CT+LDRT study median PFS were of 11 and 10 months respectively.

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<tr>
<th>Table 1: Patient's demographics</th>
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<td>Variable</td>
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<td>Median Age (range)</td>
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<td>Gross Residual Mass (%)</td>
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Conclusions: LDFRT combined to Temozolomide and hypofractionated radiation therapy is a tolerable schedule. It seems to improve outcomes when compared to hypofractionated schedule with higher dose. We have planned a new study in which Hypo-RT-CT is combined with LDRT.

**EP-1356**

**1H magnetic resonance spectroscopy for investigation of hippocampal radiation injury**

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**Purpose/Objective:** The feasibility assessment of the in vivo multivoxel magnetic resonance spectroscopy (MRS) focused on a hippocampal region as the new approach of the study of a postradiation cognitive impairment in patients with brain metastases (BM) treated by the whole brain radiotherapy (WBRT).

**Materials and Methods:** 10 patients (6 with lung, 3 with breast cancer and 1 with malignant melanoma) with BM (median 3 BM, no lesion within 5mm of hippocampus) get WBRT (2 laterolateral fields, 3000 cGy in 10 fraction) as part of palliative management. Four months after irradiation, patients underwent multivoxel MRS (Siemens Symphony, 1.5T, PRESS-CSI sequence with TE/TR = 135 ms/1690 ms, 12 averages, FOV 120×120 mm). One region of interest was placed centrically to cover the whole mesial parts of the both temporal lobes with a voxel layer inclined alongside the hippocampal long axis in order to examine whole hippocampi volume (voxel size set to 10x10x15mm). Postprocessing of raw spectroscopic data was performed utilizing LCModel (Provencher et al. 2001) for calculation of N-acetylaspartate together with N-acetyl aspartylglutamate (tNAA). tNAA are ones of commonly detectable brain tissue metabolites that are considered as the markers of neuronal density and viability. jSIPRO software (Jiru et al., 2013) was utilized for final analysis and measurement of tNAA concentration in the both hippocampi and separately its anterior and posterior portion.

**Results:** Using jSIPRO software, it was possible to evaluate tNAA concentrations within selected voxels representing the hippocampi at overlaid axial T2 image. On average 12 voxels were identified within each hippocampus, however, because of noise artifacts, 8-11 representative voxels per hippocampus were suitable for the concentration analysis. Poor-quality spectroscopic data are related especially to the anterior parts of the hippocampus because of the diverse magnetic susceptibility of surrounding fluid and bony tissues.

**Conclusions:** Besides classical single voxel MRS, multivoxel hippocampal spectroscopic imaging is feasible and well tolerated advanced MRI method for the examination of the hippocampus in patients after WBRT. For the proper calculation of particular metabolites, reading software enabling individual voxels selection is necessary since MRS from the parts of the anterior hippocampus in the proximity of lateral ventricles and bones are biased as proven in our study. Care must be taken in selection representative voxels. Basic research focusing on metabolite changes within the hippocampus after WBRT may bring more light into processes responsible for a brain radiation injury. Such results may provide more evidence for special approaches leading to a brain injury preservation as is currently widely discussed in the hippocampal avoidance whole brain radiotherapy or in a pharmacotherapy by memantine for example.

**EP-1357**

**GammaKnife Radiosurgery in the management of single and multiple brain metastases**

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