Purpose or Objective: Whole brain radiotherapy (WBRT) has been the treatment of choice for patients with brain metastases. However, change/decline of neurocognitive functions (NCFs) resulting from impaired hippocampal neurogenesis might occur after WBRT. It is reported that hippocampal sparing would provide the preservation of NCFs. Our study aims to investigate the correlations between hippocampal dosimetry and neurocognitive outcomes in patients receiving hippocampal sparing during WBRT (HS-WBRT).

Material and Methods: Fifty prospectively recruited cancer patients underwent HS-WBRT for therapeutic or prophylactic purposes. Before receiving HS-WBRT, all participants received a battery of baseline neurocognitive assessment, including memory, executive functions and psychomotor speed. The follow-up neurocognitive assessment at 4 months after HS-WBRT was also performed. To deliver HS-WBRT, Volumetric Modulated Arc Therapy (VMAT) with two full arcs and two non-coplanar partial arcs were employed. For each treatment planning, dose volume histograms were generated for left hippocampus, right hippocampus, and the composite hippocampal structure respectively. Biologically equivalent doses in 2-Gy fractions (EQD2) assuming an alpha/beta ratio of 2 Gy were computed. To perform analyses addressing the correlation between hippocampal dosimetry and the change in NCF scores, pre- and post-HS-WBRT neurocognitive assessments were available in 32 patients.

Results: NCF scores were quite stable before and after HS-WBRT regarding hippocampus-dependent memory. For verbal memory, the corresponding EQD2 values of 0%, 10%, 50%, 80% irradiating the composite hippocampal structure with -12.60Gy, -8.81Gy, -7.45Gy and -5.83Gy respectively were significantly associated with neurocognitive preservation indicated by the immediate recall of Word List Test of neuropsychological tests. The statistically significant decrease was observed in the right (-11.4%; 95% confidence interval -15.9 to -7.3; p<0.0003) as well as in the left (-8.5%; 95% confidence interval -14.0 to -3.0; p<0.0003) hippocampus.

Conclusion: Hippocampal MR spectroscopy is feasible and sensitive method for non-invasive measurement of brain radio injury. In our study, we observed correlation between left hippocampal N-acetylaspartate concentration and verbal memory decline with smaller effect of right hippocampus. Robust analysis of pre-irradiation imaging studies may provide valuable predictive biomarkers for decision making for the best radiotherapy approach in the treatment of brain metastases.

OC-0351 MRI-guided brachytherapy in cervical cancer: high doses to small bowel don’t predict late morbidity
C. Petit1, R. Mazeron1, C. Chargari1, I. Dumas1, P. Maroun1, P. Annede1, T. Seisen1, C. Haie Meder1
1Gustave Roussy, Radiation Oncology, Villejuif, France

Purpose or Objective: To establish dose-volume effect correlations for late small bowel toxicities in patients treated for locally advanced cervical cancer with concurrent chemoradiation following by MRI-guided adaptive brachytherapy.

Material and Methods: In a cohort of patients treated in curative intent and followed prospectively, those who had completed the treatment one year before were retained for this study. The small bowel loops were delineated during the planning process, but no specific dose constraint was applied. The dosimetric data, converted in 2 Gy equivalent (a/b=3) were confronted to the occurrence of small bowel events: diarrhea, pain, flatulence, bleeding, obstruction, and fistula. Patients were followed every 3 months for the first year then every 6 months, for 3 years, then annually. Late morbidity was defined over the threshold of 90 days from treatment initiation and assessed using the CTC-AE 3.0. Patients who experienced recurrences were censored from the date of their relapse. Dose-effect relationships were assessed using

OC-0349 Hippocampal dosimetry predicts the change in neurocognitive functions after whole brain radiotherapy
1Chang Gung Memorial Hospital, Department of Radiation Oncology, Taoyuan, Taiwan
2Chang Gung University, Division of Clinical Psychology-Master of Behavioral Sciences-Department of Occupational Therapy, Taoyuan, Taiwan
3Chang Gung Memorial Hospital, Department of Neurosurgery, Taoyuan, Taiwan

Purpose or Objective: After whole brain radiotherapy (WBRT), however, further basic research focusing on in-vivo description of radiation injury processes is still needed. Using magnetic resonance spectroscopy (MRS), it is possible to

measure specific metabolite concentrations in any region of interest in the brain. N-acetylaspartate (NAA) represents a marker of viable neurons. To describe hypothesized post-WBRT neuronal depletion in hippocampus, we prospectively measured changes in NAA concentrations 4 months after WBRT.

Material and Methods: Patients referred for WBRT with favorable prognosis estimated by graded prognostic assessment and without MRI hippocampal pathology were eligible for study enrollment. Before standard WBRT (two-dimensional planning, 2 laterolateral 6 megavoltage fields, dose 10x3.0 Gy delivered by linear accelerator), hippocampal spectroscopy was performed using GE Medical Systems Discovery MR 750 3T. Regional of interest was placed through the whole temporal lobi with the voxel layer position adjusted based on the localization of hippocampi. Specialized software was utilized for measurement of absolute NAA concentration in voxels within right, left and both hippocampi. The control MRS with the same setup parameters was performed 4 months after the end of course of WBRT. Wilcoxon’s signed rank test was employed for calculation of NAA concentration changes.

Results: Thirty-five patients (68% mens, mean age 59.5) were enrolled and underwent baseline MRS while only 18 (51%) of them finished the whole protocol with control measurement (15 died before and 2 refused). The most common primary cancer was lung (44%), kidney (20%) and breast (15%). On average, 9 voxels were analyzed per right and left hippocampus. The mean NAA concentration pre- and post-WBRT was 8.47 [mM] and 7.43 [mM] for the right and 8.80 [mM] and 8.04 [mM] for the left hippocampus, respectively. The statistically significant decrease was observed in the right (-11.4%; 95% confidence interval -15.9 to -7.3; p<0.0003) as well as in the left (-8.5%; 95% confidence interval -14.0 to -3.0; p<0.0003) hippocampus.

Conclusion: Hippocampal MR spectroscopy is feasible and sensitive method for non-invasive measurement of brain radio injury. In our study, we observed correlation between left hippocampal N-acetylaspartate concentration and verbal memory decline with smaller effect of right hippocampus. Robust analysis of pre-irradiation imaging studies may provide valuable predictive biomarkers for decision making for the best radiotherapy approach in the treatment of brain metastases.

Proffered Papers: Brachytherapy 4: Gynae-Breast

OC-0350 Post-radiation neuronal depletion in hippocampus measured by in-vivo magnetic resonance spectroscopy
P. Pospisil1, T. Kazda2, R. Jancaíek3, P. Slampa1
1Masaryk Memorial Cancer Institute, Radiation Oncology, Brno, Czech Republic
2St. Anne’s University Hospital Brno, Department of Neurosurgery, Brno, Czech Republic

Purpose or Objective: Ongoing clinical trials are evaluating advantage of hippocampal avoiding whole brain radiotherapy (WBRT), however, further basic research focusing on in-vivo description of radiation injury processes is still needed. Using magnetic resonance spectroscopy (MRS), it is possible to
mean dose comparisons (T-pair and Kruskal-Wallis tests), log rank tests on event-free survivals, and probit analyses. The highest graded event, or in cases of similar grade the earliest, was considered for analyses.

Results: One hundred and fifteen patients were eligible. Of them, 94.8% received concomitant chemoradiotherapy; 12.2% extended-field radiotherapy, and 32.2% nodal sequential boost. Their mean age was 47.5 years. The median follow-up was 35.5 months. A total of 522 events was reported. Focusing on the highest grade per patient: 17 had grade 0, 75, grade 1, 20, grade 2 and 3, grade 3. The prevalence of grade 1 events appeared stable during the study period, ranging between 31.2 and 50%. The one of grade 2 events tended to worsen: 2.2% at 6 months, 4.5% at 1 year, 6.9% at 2 years, and 7.0% at 3 years. Incidences of grade 2-4 events were 0.9% at 6 months, 6.6%, 19.0%, and 27.2% at 1, 2, 3 years respectively. The mean D2cm3 and D0.1cm3 were respectively 68.7±13.6 Gy and 85.8±33.1 Gy and did not differ according to grade (p=0.47 and p=0.50). Comparisons of mean D2cm3 and D0.1cm3 according to grade 0-1 versus 2-4 were not significant (68.0±12.4 vs 71.4±17.7 Gy, p=0.38 and 83.7±26.4 vs 94.5±51.9 Gy, p=0.33 respectively). Log rank tests were performed after splitting patients into 4 groups according to D2cm3 levels: > 80 Gy, 70 to 79 Gy, 60 to 70 Gy and < 60 Gy. No difference was observed for grade 1 events (p=0.52), grade 2-4 (p=0.52) or grade 3-4 (p=0.21). Probit analyses showed no correlation between both dosimetric parameters and the probability of small bowel events grade 1-4, 2-4, or 3-4 (p ranging from 0.19 to 0.48).

Conclusion: No significant dose-volume effect relationships were demonstrated between the D2cm3 and D0.1cm3 and the probability of late small bowel morbidity. These two parameters should not limit the optimization process.

OC-0352
The high doses employed in brachytherapy of cervical cancer counteract hypoxia - a modelling study
E. Lindblom, A. Dasu, I. Toma-Dasu
Stockholm University, Medical Radiation Physics, Stockholm, Sweden
Linköping University, Department of Radiation Physics and Department of Medical and Health Sciences, Linköping, Sweden
Stockholm University and Karolinska Institutet, Medical Radiation Physics, Stockholm, Sweden

Purpose or Objective: Brachytherapy is a well-established radiotherapy treatment modality that has been employed in treatments of several cancer types for more than a century. One of the most common treatment strategies for cervical cancer today is a combination of external beam radiotherapy, chemotherapy and brachytherapy. Similar to other forms of radiation therapy, pre-treatment imaging of hypoxia is rarely done for cervical cancer. Nevertheless, the clinical outcome is highly positive, despite the fact that hypoxia has been repeatedly confirmed in cervical tumours. It was therefore the purpose of this study to investigate whether the success of brachytherapy in these tumours, seemingly regardless of oxygenation status, could be explained by the characteristics of the brachytherapy dose distributions in comparison to external beam radiotherapy.

Material and Methods: A previously used in silico model of tumour oxygenation and radiation response was further developed to simulate the treatment of cervical cancer employing the combination of external beam radiotherapy and intrauterine brachytherapy. Based on the local clinical protocol and using a clinically derived brachytherapy dose distribution and assuming a homogeneous dose delivered by external radiotherapy, survival was assessed on voxel level taking into account the dose-modifying effect of the oxygenation as well as the effects of repair and repopulation of tumour cells during treatment. Two scenarios were considered for brachytherapy: one in which the high dose region was highly conformal to the hypoxic region in the target and one in which they were displaced relative to each other. Overall-response was assessed as Poisson-based tumour control probability (TCP). The interplay between tumour oxygenation and the heterogeneous high-dose distribution was also studied by simulating different spatial and temporal patterns of hypoxia. The results were compared to the case when irradiation was performed only with external beams delivering a homogenous dose to the target.

Results: Predicted values of D50 with respect to the external treatment and assuming reoxygenation were in agreement with the clinically observed high cure rates. Assuming fast reoxygenation, the D50 was similar for the different cases of overlap between the brachytherapy dose distribution and the tumour, regardless if the hypoxic fraction was 10% or 25% (Table 1). To achieve 95% control with external RT only, a total dose of more than 70 Gy in 25 fractions would be required for both cases of hypoxic fraction assuming reoxygenation (Figure 1).

Conclusion: Assuming fast reoxygenation, the dependence on the degree and extent of hypoxia has little impact on the outcome and therefore the high doses delivered in brachytherapy could counteract the negative impact of hypoxia.

OC-0353
EBRT and interstitial brachytherapy for recurrent vault carcinomas: Factors influencing the outcomes
1Tata Memorial Centre, Surgical Oncology, Mumbai, India
2Tata Memorial Centre, Radiation Oncology, Mumbai, India

Purpose or Objective: Post hysterectomy vaginal vault recurrences have poor outcomes with pelvic control rates ranging from 50-60%. We conducted this prospective study at our centre with an aim to determine the factors influencing...