

Impact of ^{18}F -FET PET on Target Volume Definition and Tumor Progression of Recurrent High Grade Glioma Treated with Carbon-Ion Radiotherapy

Charlotte Debus^{1-4,#}, Maria Waltenberger¹⁻⁴, Ralf Floca^{3,5}, Ali Afshar-Oromieh⁶,
Nina Bougati^{3,4}, Sebastian Adeberg^{3,4}, Sabine Heiland⁷, Martin Bendszus⁷, Wolfgang Wick^{1,8}, Stefan
Rieken^{3,4}, Uwe Haberkorn^{6,9}, Jürgen Debus¹⁻⁴, Maximilian Knoll¹⁻⁴, and Amir Abdollahi^{1-4,#}

¹German Cancer Consortium (DKTK), Heidelberg, Germany

²Translational Radiation Oncology, National Center for Tumor Diseases (NCT), German Cancer Research Center (DKFZ), Heidelberg, Germany

³Division of Molecular and Translational Radiation Oncology, Heidelberg Institute of Radiation Oncology (HIRO), National Center for Radiation Research in Oncology (NCRO), Germany

⁴Heidelberg Ion-Beam Therapy Center (HIT), Department of Radiation Oncology, Heidelberg University Hospital, Germany

⁵Software development for Integrated Diagnostics and Therapy, German Cancer Research Center DKFZ), Heidelberg, Germany

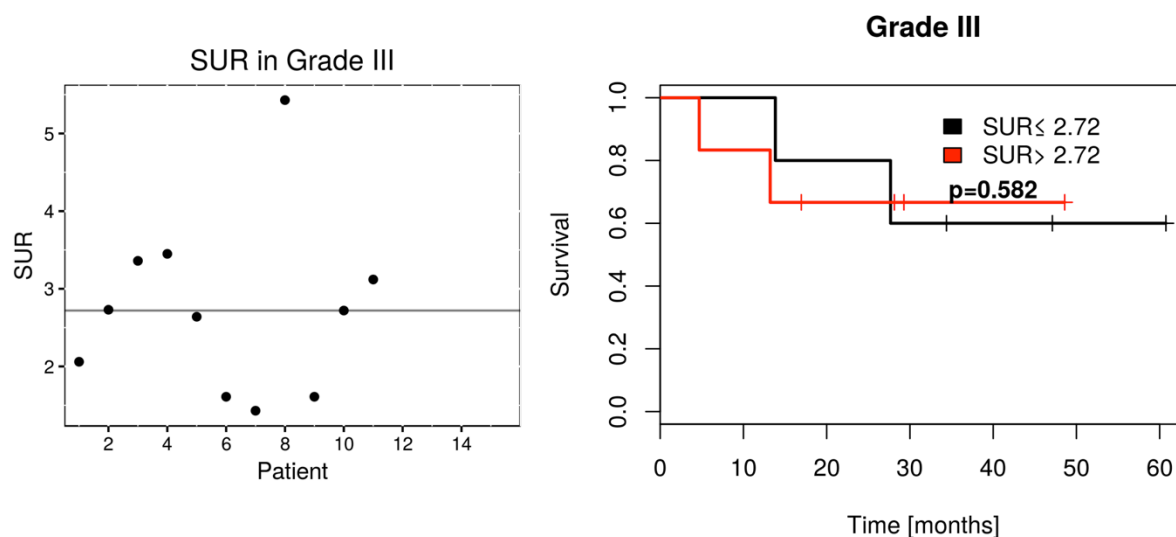
⁶Department of Nuclear Medicine, Heidelberg University Hospital, Germany

⁷Department of Neuroradiology, Heidelberg University Hospital, Germany

⁸Department of Neurology, Heidelberg University Hospital and Clinical Cooperation Unit Neurooncology, National Center for Tumor Diseases (NCT), German Cancer Research Center (DKFZ), Heidelberg, Germany,

⁹Clinical Cooperation Unit Nuclear Medicine, German Cancer Research Center DKFZ), Heidelberg, Germany

Supplements



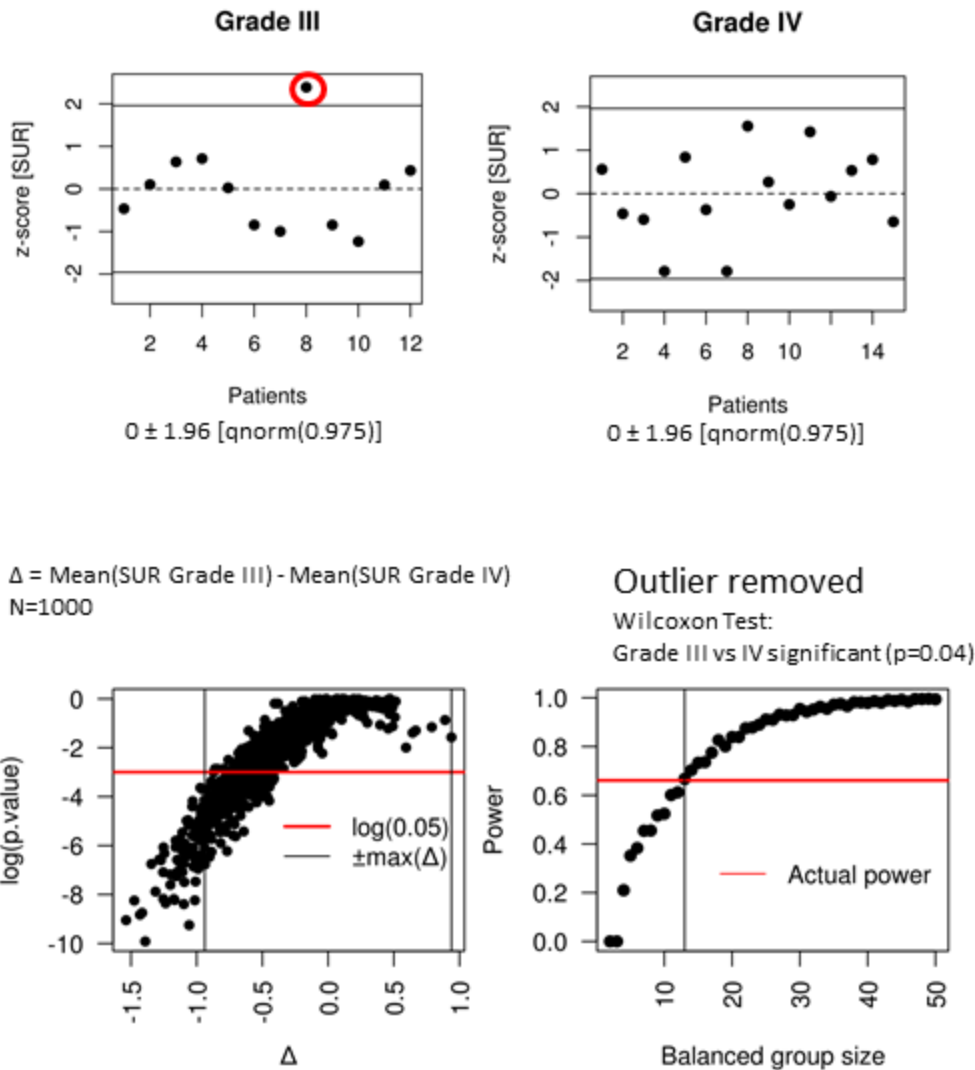
Supplementary figure 1: Relation between SUR and Survival in grade III glioma. The median value of SUR=2.72 separated two groups. However, the differences between the two groups were statistically not significant (log-rank, $p=0.582$). Overall, the median survival was not reached in both groups and the number of patient was limited for a decisive conclusion.

Correlation with		All	Grade III	Grade IV
SUV _{max}	Pearson	0.31	0.22	0.43
	Spearman	0.31	0.2	0.42
SUR	Pearson	0.21	0.11	0.35
	Spearman	0.29	0.05	0.56

Supplementary table 1: Correlation coefficients R for relationship between SUV_{max}/SUR with the maximum conformity index CI_{max} (c.f. Fig. 3c)

Sensitivity analysis & power calculation:

SUR was slightly but not significantly higher in grade IV glioma compared to grade III glioma.

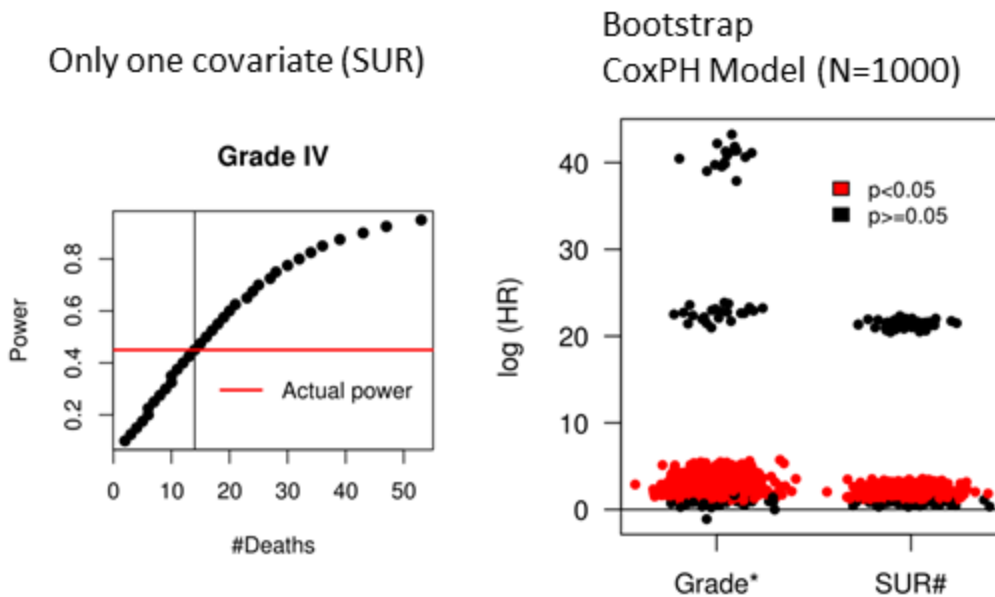


→ SUR Grade III < SUR Grade IV

Supplementary figure 2: Sensitivity analysis of the SUR difference between grade III and IV tumors. Potential outliers in SUR measurements were identified by examination of standardized values (z-transformation). Calculation of effect differences between groups and the corresponding Wilcoxon p-value (two-sided) for 1000 bootstrapped datasets (including the outlier). Post-ho power calculation using the observed measurements (outlier removed) for a balance group design.

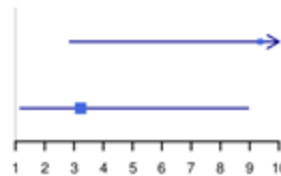
Power calculation

In grade IV tumors, the median value of SUR=2.92 clearly separated patients into two prognostic subgroups as shown in KM-plot.



Multivariate: Grade + SUR

	Hazard Ratio	95% CI	p-value
Grade*	9.36	2.85-30.76	<0.001
SUR#	3.22	1.16-8.95	0.025



Two covariates: Grade + SUR

Required number of deaths: 34

* Grade IV vs III
high vs low

Supplementary figure 3: Multivariate survival analysis (tumor grade and SUR) for the observed and bootstrapped data as well as power and sample size calculation using estimates derived from the presented data