NMN Symposium 2024 – Abstract Book

Abstract Number: 8
Abstract Title: ***Correlations of 18F-DOPA PET metrics with the Ki-67 proliferation labeling index in gliomas***

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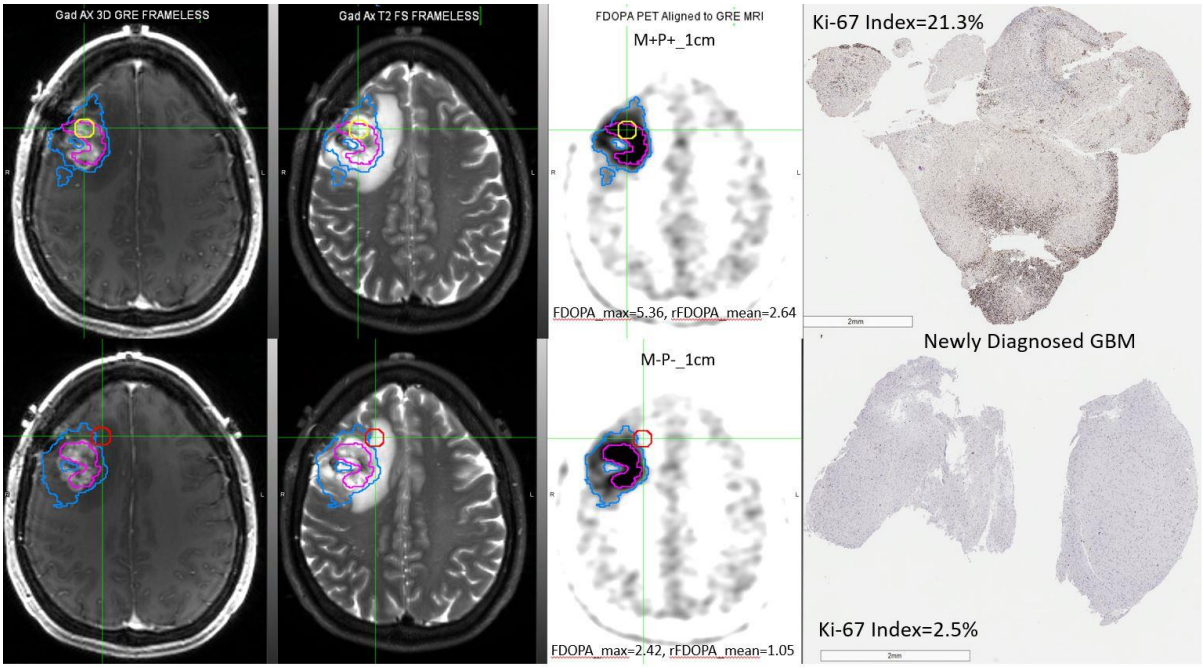
Background:
According to the World Health Organization (WHO), tumor grade is a powerful prognostic factor for gliomas. The 2016/2021 refinement of the CNS WHO grade classification, uses integrated phenotypic and genotypic parameters. Studies suggest Ki-67 be used as an ancillary marker for glioma grading. Inadequate tissue for grading and quantifying Ki-67 index, along with tumor heterogeneity and sampling errors, create a clinical need for a noninvasive imaging tool to predict pathologic characteristics used in formulating tumor grade.
Material and Methods:
Under two prospective clinical trials between October 2010 and January 2019, 252 stereotactic biopsies (MC1078 n=50, MC1373 n=202) across 79 patients (MC1078 N=21, MC1373 N=58) were collected under MRI guidance with registered 3,4-dihydroxy-6-[18F] fluoro-L-phenylalanine (18F-DOPA PET/CT) from brain tumor patients (Table 1). All biopsy samples were stained for Ki-67 expression. Ki-67 index was computed as the percent of Ki-67 positive nuclei per total nuclei. Spearman correlations were computed between mean FDOPA SUV relative to normal brain (rFDOPA mean) and Ki-67 index.
Results:
Figure 1 illustrates examples of biopsy locations on MR and FDOPA imaging and the corresponding Ki-67-stained biopsy samples. Table 2 summarizes Spearman correlation results for all samples and by histologic and disease status subgroups. There was a significant positive monotonic relationship between rFDOPA mean and Ki-67 index for both recurrent (rho=0.408, $p<0.001$) and newly diagnosed (rho=0.674, $p<0.001$) astrocytomas, as well as recurrent oligodendrogliomas (rho=0.697, $p<0.001$). The correlation was non-significant for newly diagnosed oligodendrogliomas (rho=0.216, $p=0.193$).
Conclusion:
These results demonstrate an initial look into the utility of FDOPA imaging as a predictor of a pathologic characteristic. Our analysis shows relative FDOPA SUV values are positively correlated with Ki-67 index. Future analysis will provide further information on the ability of FDOPA to predict tumor grade, histologic type, newly diagnosed or recurrent, IDH type, and additional pathology.

Table 1. Patient and sample characteristics by study

Patient Characteristics	MC1078	MC1373	Total	p-value
Number of patients	21	58*	79	
Sex				
Male n (%)	14 (66.7)	33 (56.9)	47 (59.5)	0.6046[1]
Female n (%)	7 (33.3)	25 (43.1)	32 (40.5)	
Age, median (range)	39 (20 – 69)	46.5 (7 – 76)	46 (7 - 76)	0.3150[2]
Disease Status				
Newly diagnosed n (%)	15 (71.4)	27 (46.6)	42 (53.1)	0.0737[1]
Recurrent n (%)	6 (28.6)	31 (53.5)	37 (46.8)	
2016 WHO Classification				
Grade II	5 (23.8)	15 (25.9)	20 (25.3)	0.3231[1]
Grade III	11 (52.4)	20 (34.5)	31 (39.2)	
Grade IV	5 (23.8)	23 (39.7)	28 (35.4)	
Samples per patient, median (range) Mean (SD)	2 (1 – 5) 2.4 (0.97)	3 (1 – 12) 3.5 (1.98)	3 (1 – 12) 3.2 (1.83)	0.0059[2]
Sample Characteristics	**MC1078**	**MC1373**	**Total**	**p-value**
Number of samples	50	202	252	
Sample type**				
Biopsy n (%)	13 (26)	51 (25.2)	64 (25.4)	1.0000[1]
Resection n (%)	37 (74)	151 (74.8)	188 (74.6)	
Histopathology (WHO 2016)				
Oligodendroglioma n (%)	13 (26.0)	50 (24.8)	63 (25.0)	0.9404[1]
Astrocytoma n (%)	37 (74.0)	148 (73.3)	185 (73.4)	
Indeterminate n (%)	0 (0)	4 (2.0)	4 (1.6)	
IDH mutation status				
Mutant n (%)	30 (76.9)	113 (58.2)	143 (61.4)	0.0312[1]
Wildtype n (%)	9 (23.1)	81 (41.8)	90 (38.6)	
Missing	11	8	19	

*MC1373 Two patients were enrolled twice, once with newly diagnosed and once with recurrent disease; age and disease status reflect status at first enrollment. WHO classification remained the same for both patients.
**Patient FDOPA44 on MC1373 had both biopsy (n=1) and resection (n=2) samples
1 Exact p-value
2 Kruskal-Wallis p-value

Table 2. Spearman correlation coefficients for relative mean FDOPA uptake versus Ki-67 index among all samples and by disease status and histology subgroups		
	Spearman's Rho	P value
All samples (n = 248)	0.502	<0.001
Newly diagnosed samples (n = 116)	0.548	<0.001
Recurrent samples (n = 132)	0.479	<0.001
Astrocytoma only samples (n = 185)	0.446	<0.001
Newly Diagnosed astrocytoma (n = 78)	0.674	<0.001
Recurrent astrocytoma (n = 107)	0.408	<0.001
Oligodendroglioma only samples (n = 63)	0.526	<0.001
Newly Diagnosed oligodendroglioma (n = 38)	0.216	0.193
Recurrent oligodendroglioma (n = 25)	0.697	<0.001



Author Disclosures:
D.H. Pafundi: None. **M. Zakhary:** None. **I. Parney:** None. **C. Giannini:** None. **T. Burns:** None. **C. Hunt:** None. **V. Lowe:** None. **Y. Zhang:** None. **S.K. Anderson:** None. **M. Seaberg:** None. **H. Wan Chan Tseung:** None. **N. Laack:** None. **D. Brinkmann:** None.

Abstract Number: 9
Abstract Title: ***Promising theranostic targets for high-grade pediatric central nervous system tumors***

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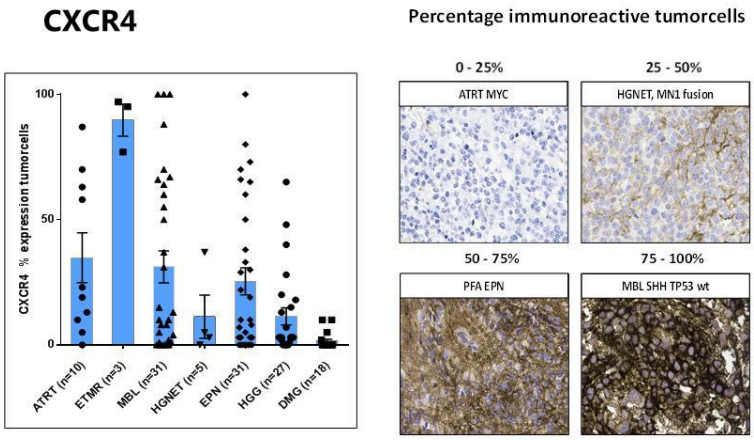
Background:
Pediatric high-grade brain tumors (pHGBT) are the leading cause of childhood cancer-related death, and the majority of pHGBT patients show poor response to standard therapies. This demands new treatment strategies, such as theranostics. Here, we have analyzed expression of promising theranostic targets in pHGBT.
Material and Methods:
We studied protein levels and mRNA expression of CD276 (encoding B7H3), CXCR4, FAP, FOLH1 (encoding PSMA) and SSTR2a in a cohort from the Princess Maxima Center (n=124), consisting of medulloblastomas, ATRTs, ependymomas and high-grade gliomas. Protein levels were analyzed by immunohistochemistry, and expressed as H-score (multiplication of percentage of cells with intensity score). Correlations were performed using Spearman's rank test.
Results:
B7H3 and CXCR4 showed highest expression in pHGBT samples, with quite some interpatient variability. SSTR2a expression was mainly seen in medulloblastoma and in a few ependymoma and HGG samples. PSMA and FAP showed almost no expression on pHGBT. When analyzed by tumor type, embryonal tumors displayed expression of most theranostic targets, while diffuse midline gliomas showed the lowest target expression, with only (weak) B7H3 expression in 50% of cases. There was no significant correlation with patients age, tumor location, epigenetic subclass or molecular tumordriver. There was a strong mRNA-protein correlation for SSTR2a (rho 0.85) and PSMA (rho 0.98). For B7H3 (rho 0.38) and CXCR4 (rho 0.54) correlations were moderate, and for FAP there was no correlation.
Conclusion:
B7H3 and CXCR4 are the most promising theranostic targets for pHGBT. SSTR2a is the most relevant target for medulloblastoma. Based on the variable mRNA-protein correlations, immunhistochemistry seems most suitable for identifying patients that may benefit from radionuclide therapy. Further research should focus on producing radiopharmaceuticals for radionuclide therapy targeting B7H3 and CXCR4 for pediatric CNS tumors, with a special focus on the ability to cross the blood brain barrier, and studying PET-uptake in patients.



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Abstract Number: 10
Abstract Title: ***^{68}Ga/^{177}Lu-PSMA theranostics in recurrent high-grade glioma - first study results***

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Background:
In the current study, ^{68}Ga/^{177}Lu-PSMA theranostics is evaluated as a treatment alternative to improve existing diagnostic and therapeutic methods in glioma management, and possibly increase the overall survival and quality of life for this patient group.
Material and Methods:
Eligible patients with a positive ^{68}Ga-PSMA-PET/MRI examination are selected for 177Lu-PSMA treatment (maximum 6 cycles, 6-8 weeks intervals). The patients are carefully monitored during each treatment cycle (PET/MR, SPECT/CT, neurological tests, blood tests, and quality of life questionnaires). Two patients with CNS WHO grade 4 glioblastomas have been included in this ongoing study. Both patients received standard treatment with surgery, radiotherapy and chemotherapy prior to inclusion, and were left with no other treatment options at recurrence. 177Lu-PSMA (7.1-7.3 GBq) was administered intravenously (Patient A: 1 treatment, Patient B: 3 treatments) and SPECT/CT scans were performed for dosimetry.
Results:
^{68}Ga-PSMA-PET prior to treatment demonstrated tumor uptake in both patients (SUV_{max_A}:9.0 and SUV_{max_B}:4.4) as well as uptake in the parotid glands (SUV_{max_A}:21.8 and SUV_{max_B}:15.9). ^{68}Ga-PSMA uptake in normal brain was low, yielding high TBR (TBR_A:136.0 and TBR_B:45.4). Post treatment SPECT/CT revealed a rapid wash-out of activity, resulting in low absorbed doses (A: Tumor 1.4 Gy, kidneys 2.0-2.1 Gy, parotid glands 1.1-1.4 Gy, B: Tumor 2.6-2.9 Gy, kidneys 2.4-3.7 Gy, parotid glands 1.7-3.6 Gy). The patients reported no subjective side effects of the treatment, apart from transient xerostomia. Based on radiological evaluation (MRI), both patients demonstrated stable disease during the treatment cycles (third cycle not yet evaluated).
Conclusion:
Despite low tumor doses, the radiological stability of disease in these two patients is promising. An innovative approach to boost brain tumor doses is to use intraarterial administration instead of intravenous administration. We will now apply for a change in the study protocol for the possibility to use this method in selected patients.

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Abstract Number: 12

Abstract Title: ***Development of [^{18}F]AG-120 as radiotracer for the detection by positron emission tomography (PET) of the mutant isocitrate dehydrogenase 1 in glioma***

Authors:
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Background:
Mutations of isocitrate dehydrogenase (IDH) enzymes are frequent alterations in glioma - the most common being the IDH1R132H - and their identification has become essential for patient stratification. Here, we propose a transdisciplinary approach to develop an ^{18}F-labeled ligand to detect the IDH1R132H protein directly and non-invasively by PET.
Material and Methods:
Radiosynthesis was performed using the TRACERlab FX2 N automated radiosynthesizer. *In vitro* evaluation of inhibitory potency, binding affinity, and cell uptake of [^{18}F]**AG-120** was performed using U251 human glioblastoma cells stably transfected with IDH1 or IDH1R132H. *In vivo* metabolism was investigated in CD-1 mice, and dynamic PET scans (NanoScan®PET/CT) were performed in nude rats bearing U251-IDH1 or U251-IDH1R132H glioblastoma.
Results:
AG-120 shows a high inhibitory potency toward IDH1R132H (IC_{50}=5.11 nM). Diastereomerically pure [^{18}F]**AG-120** was produced by an automated copper-mediated radiofluorination. Internalization studies showed a higher uptake of [^{18}F]**AG-120** in U251-IDH1R132H cells compared to that in U251-IDH1 cells (0.4 vs. 0.013% ID/µg protein at 120 min), which was suppressed by self-blocking (0.009% ID/µg protein at 120 min). Excellent metabolic stability *in vivo* was demonstrated (parent fractions in plasma and brain at 30 min p.i.: 85% and 91%, respectively). Low initial uptake in tumors of both models (TAC-peak value ~0.4 SUV) was observed. A slightly higher retention in IDH1R132H- compared to IDH1-tumors (Tumor-to-Background Ratio[30-60min]: ~1.6 *vs.* ~1.1) was detected.
Conclusion:
We have successfully automated the production of [^{18}F]**AG-120** and gained valuable insights into its interactions with IDH1 and IDH1R132H. [^{18}F]**AG-120** will serve as a reference compound for future evaluations of mIDH inhibitors/radioligands and may have applications in peripheral tumors, such as

chondrosarcoma.

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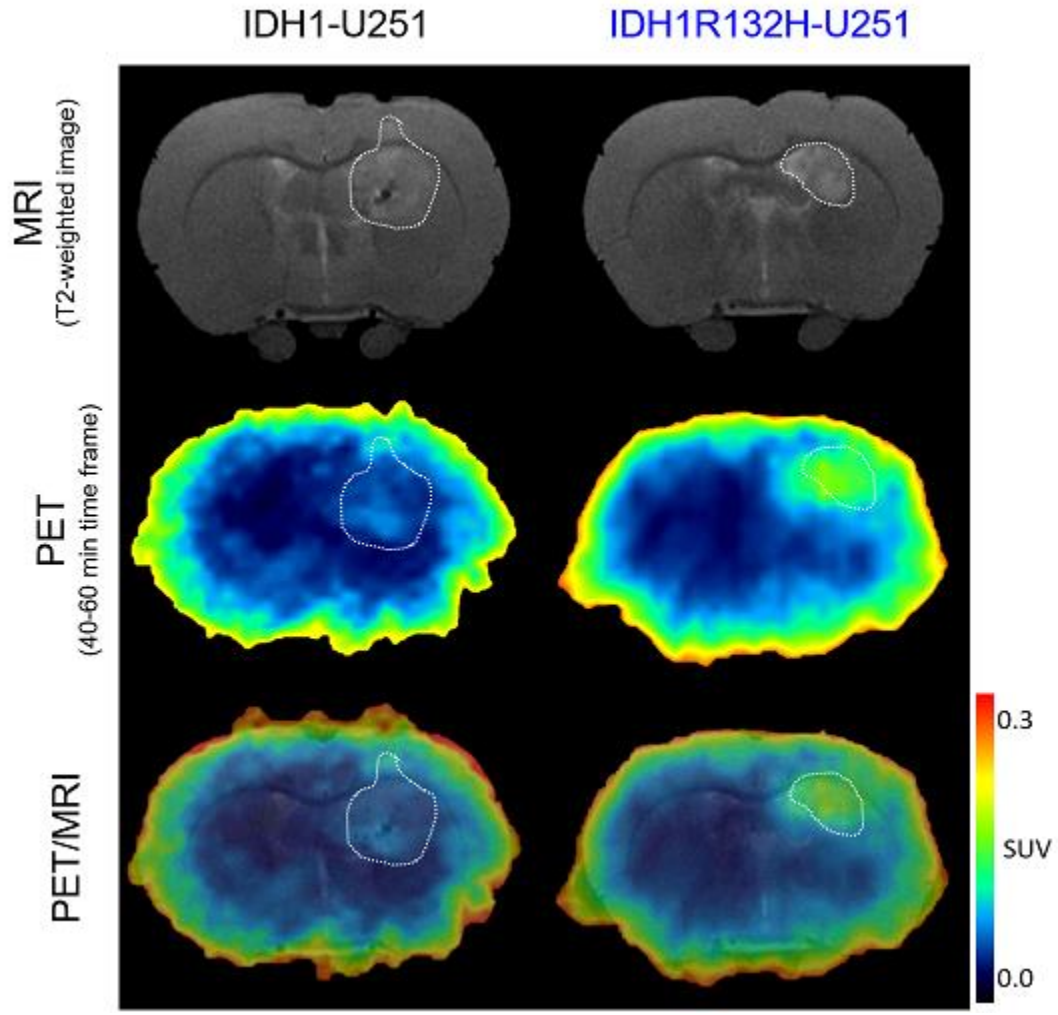

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Abstract Number: 13
Abstract Title: ***Multi-site, prospective trial evaluating FET-PET In Glioblastoma (FIG) Study (TROG 18.06): Central review of initial FET-PET biologic target volume delineation for radiation planning.***

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Background:
To provide 1) a 'trials in progress' update from the multi-site trial evaluating O-(2-[18F]-fluoroethyl)-L-tyrosine Positron Emission Tomography (FET-PET) in Glioblastoma (FIG) study and 2) assess the preliminary impact of central Nuclear Medicine physician (NMP) review of prospective FET-PET1 delineation of the biological target volume (BTV) for radiotherapy (RT) planning.
Material and Methods:
Up to 210 adult GBM participants across 11 Australian sites will undergo FET-PET post-surgery/pre-chemo-RT [CRT] (FET-PET1), one month post CRT (FET-PET2) and at suspected progression (FET-PET3). Group 1 participants enter pre-CRT at timepoint 1 (FET-PET1 with MRI1), whilst Group 2 enter at timepoint 2. Adjuvant RT target volumes are derived per standard contrast MRI with hybrid post-hoc RT volumes created by incorporating the FET-PET1 NM-derived BTV utilising a trial-specific MiM version 7.0 workflow. All trial sites and NMP have passed credentialling including three benchmarking cases per NMP involving Static gross target volume (GTV) and BTV delineation.
Results:
Trial recruitment commenced in January 2021, with 170 (n=107 Group 1 and n=63 Group 2) participants currently enrolled, with a target of 140 Group 1 participants. During trial credentialling, results demonstrated protocol variations in FET-PET1-derived BTV in 25/72 (34.7%) - 13 minor and 12 major. During prospective recruitment, 4/25 (16.0%) FET-PET1 with BTV delineation cases after central review required resubmission, for reasons including incorrect imaging sequence selection within the MiM workflow (n=2) and both MiM

workflow issues and Static GTV overcontouring (n=2).

Conclusion:

The FIG trial will complete recruitment in 2024 with analyses planned at one year post CRT completion. Despite improvements in resubmission rates compared to the credentialling phase, central review of prospective FET-PET1-derived BTV delineation remains important in ensuring protocol adherence. The FIG study is the largest prospective multi-site study addressing FET-PET's impact on adjuvant RT planning and its role in management of pseudoprogression and prognostication.

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Abstract Number: 14
Abstract Title: ***Evaluation of the Utility of PET Imaging Based on WHO Classification 5th edition for Brain Tumor Diagnosis***

Authors:
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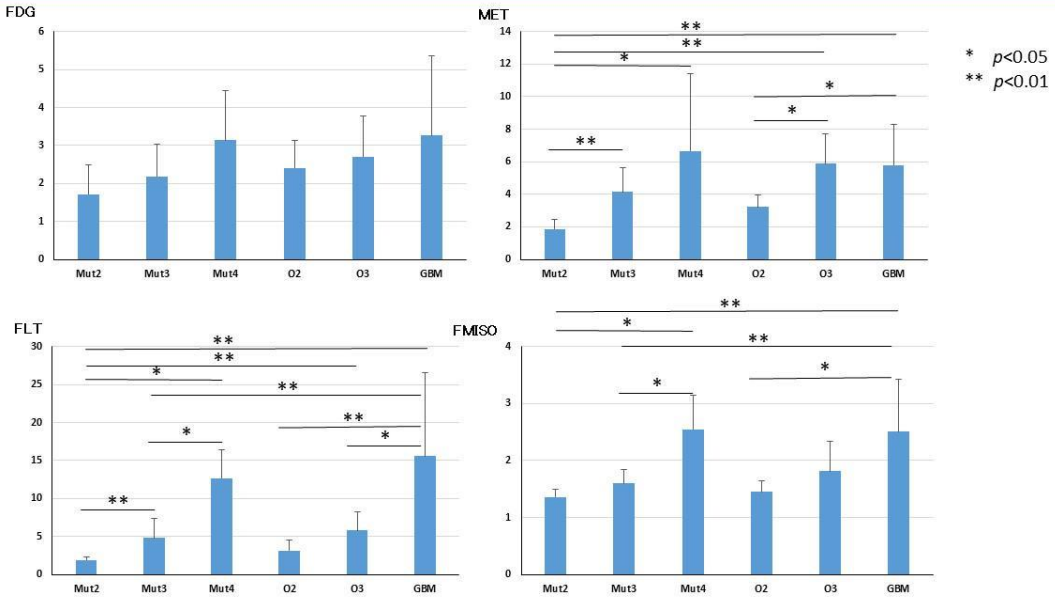
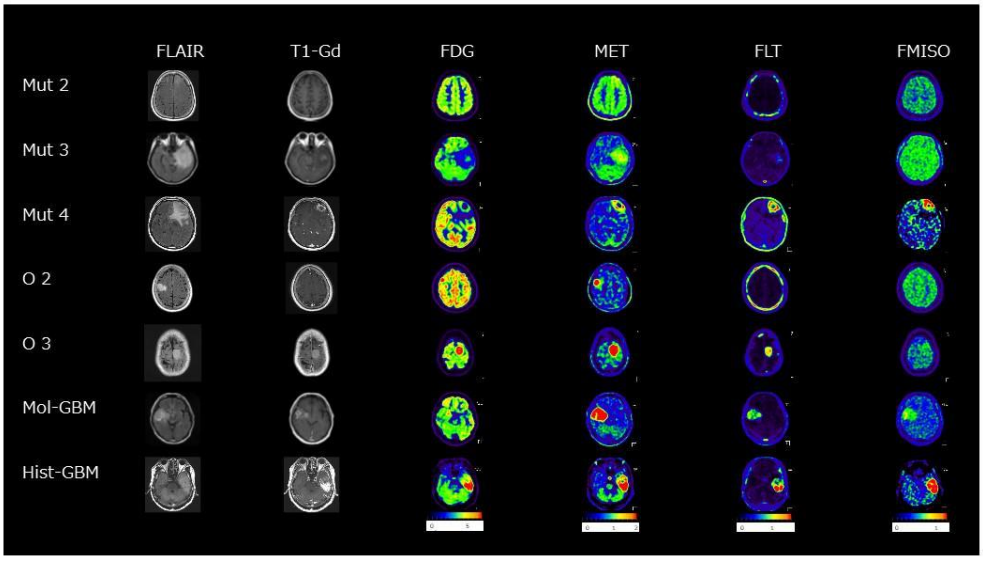
Background:
Diagnosing brain tumors and assessing treatment effectiveness solely with MRI can be challenging. This study aims to investigate the utility of PET examinations in diagnosing brain tumors according to the 5th edition of the WHO brain tumor classification.
Material and Methods:
A total of 380 patients with CNS diseases, including glioma (186 cases), metastatic brain tumor (73 cases), malignant lymphoma (69 cases), and meningioma (52 cases), underwent PET scans (FDG, MET, FLT, and FMISO) at our department between April 2009 and December 2023. We measured and compared tumor to normal tissue ratio (TNR) and tumor to blood ratio (TBR). Gliomas were categorized based on the WHO Classification of Brain Tumors, Fifth Edition, comparing molecular glioblastoma and histological glioblastoma, as well as with molecular glioblastoma. Metastatic brain tumors, primary central nervous system lymphoma (PCNSL), and meningioma were compared to glioblastoma.
Results:
For IDH-mut grades 2 and 4 gliomas, the TNR values were MET 2.86 and FLT 6.93. IDH-mut grade 2 gliomas and glioblastomas had TNR values of MET 2.20, FLT 2.48, and FMISO 1.52 as cutoff values. For molecular glioblastoma compared to histological glioblastoma, the TNR values were MET 4.61, FLT 7.65, and FMISO 1.71 as cutoff values. The median progression-free survival (PFS) was 21.47 months for gliomas and 10 months for glioblastomas. Metastatic brain tumors had lower TBR values than glioblastomas with cutoff values of FDG 2.26, MET 4.37, and FMISO 2.2. Malignant lymphomas had higher TBR values than glioblastomas with cutoff values of FDG 2.92 and FMISO 2.01. Meningiomas had lower TBR values than glioblastomas with FDG 1.62 as the cutoff value.
Conclusion:
PET scans, based on the WHO Classification of Brain Tumors, Fifth Edition, prove valuable in diagnosing brain tumors and evaluating treatment efficacy. They are particularly useful in classifying gliomas and distinguishing them from glioblastomas.

Multiple PET tracers for use in the classification of gliomas according to the 2021 WHO criteria



Multiple PET tracers for use in the classification of gliomas according to the WHO 2021 criteria



Author Disclosures:

K. Miyake: None. **M. Tatano:** None. **T. Kanda:** None. **K. Suzuki:** None. **D. Ogawa:** None. **T. Hatakeyama:** None.

Abstract Number: 15
Abstract Title: ***Safety of lutetium Lu 177 dotatate for recurrent meningioma with history of radiation necrosis - a case report***

Authors:
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Background:
Radiation-associated meningiomas are characterized by high rates of recurrence. Lutetium Lu 177 dotatate may represent a treatment option for these tumors but safety of this agent for patients with history of radiation necrosis is unknown.
Material and Methods:
In this case report we present preliminary safety of lutetium Lu 177 dotatate administered to a patient with history of radiation necrosis.
Results:
A patient with CNS germinoma was treated with cisplatin and etoposide followed by craniospinal irradiation (30 Gy, 20 fractions) with tumor boost (53.4 Gy, 33 fractions). Twenty years later MRI brain obtained for focal seizures demonstrated a left parietal extra-axial mass lesion within the previous irradiation field. Subtotal resection established diagnosis of CNS WHO grade 2 meningioma. He received additional radiation therapy (60 Gy, 30 fractions). Seventeen months later, tumor progression was treated with gamma knife radiosurgery (GKRS, marginal dose 15 Gy, maximum dose 30 Gy, volume 12 cc). Seven months after GKRS, patient had recurrent seizures with imaging demonstrating radiation necrosis characterized by increased enhancement and vasogenic edema. Patient was treated with bevacizumab (7.5 mg/kg, every 3 weeks, 4 doses) with resolution of edema. One year later, MRI brain demonstrated tumor progression within treatment field. Gallium Ga 68 DOTATATE positron emission tomography demonstrated that the meningioma was DOTATATE avid with Krenning score 2. Patient was treated with lutetium Lu 177 dotatate (two infusions, two months apart), which was well-tolerated with no significant toxicities and no recurrent radiation necrosis. Four months after lutetium Lu 177 dotatate initiation, patient experienced disease progression, was transitioned to bevacizumab.
Conclusion:
In this patient with history of intracranial radiation for CNS germinoma and meningioma and radiation necrosis, treatment with lutetium Lu 177 dotatate was well-tolerated. Safe lutetium Lu 177 dotatate administration may be feasible for patients who have a history of radiation necrosis.

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Abstract Number: 16
Abstract Title: ***ReSPECT-LM Phase 1 Dose Escalation Trial of Rhenium (^{186}Re) Obisbemeda (Rhenium-186 Nanoliposome, ^{186}RNL) in Leptomeningeal Metastases (LM)***

Authors:
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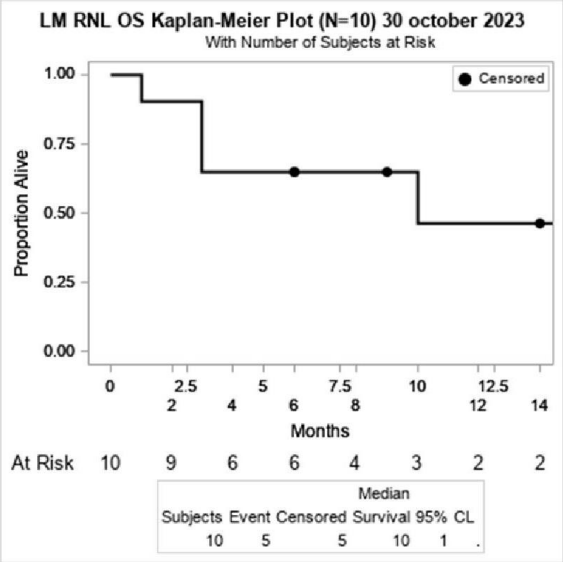
Background:
Leptomeningeal metastases (LM) are a devastating complication commonly seen with breast, lung, and melanoma, with limited treatment options and poor survival. A Phase 1 dose escalation trial was initiated to determine safety and Recommended Phase 2 Dose (RP2D) of a single administration of *186*RNL given by intraventricular catheter for LM patients. *186*RNL is nanoliposome-encapsulated rhenium-186, providing locoregional delivery of high-energy beta-particles with simultaneous gamma photon decay for real-time imaging.
Material and Methods:
3+3 modified Fibonacci design was implemented. 10 patients were treated over 3 Cohorts. The primary objective was to determine maximum tolerated dose (MTD), with secondary objectives including overall survival (OS) and progression free survival (PFS), and an exploratory endpoint to perform analysis on cerebral spinal fluid (CSF) pre- and post-treatment. Whole body planar and SPECT/CT imaging was performed for biodistribution and dosimetry.
Results:
The MTD was not reached and there were no dose-limiting-toxicities (DLTs). Most AEs were mild (58.7%) and moderate (24%). Only 8 SAEs were found; all were unrelated/unlikely-related to study drug except for one. Average absorbed doses to organs remained low while absorbed doses to ventricles and cranial subarachnoid space (24.84Gy, 40.86Gy, 63.83Gy) and spinal fluid (6.88Gy, 20.73Gy, 44.07Gy) increased with administered dose. CSF tumor cell counts showed up to 91% reduction in tumor cell count following treatment, with an average of 53% reduction at Day 28. Neurological signs and symptoms were reported to improve by investigators/patients. Median OS was 10 months (95%CI 1m).
Conclusion:
A single administration of *186*RNL in LM patients was shown to be safe and well-tolerated up to 26.4mCi. The MTD was not reached and no DLTs were observed. CSF tumor cell counts were shown to decrease post-treatment and remain durable up to 28-days. Phase 1 remains open and enrolling to determine the RP2D and further define safety and preliminary efficacy.



Author Disclosures:

A. Brenner: A. Employment (full or part-time); Significant; UT Health San Antonio - Mays Cancer Center. B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; UT Health San Antonio - Mays Cancer Center. Other; Significant; PLUS Therapeutics. **M. Youssef:** A. Employment (full or part-time); Significant; UT Southwestern Medical Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **P. Kumthekar:** A. Employment (full or part-time); Significant; Northwestern Medicine. Other; Modest; PLUS Therapeutics. **A. Bao:** A. Employment (full or part-time); Significant; Case Western Reserve University. Other; Modest; PLUS Therapeutics. **W. Phillips:** A. Employment (full or part-time); Significant; UT Health San Antonio - Mays Cancer Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **J. Michalek:** A. Employment (full or part-time); Significant; UT Health San Antonio - Mays Cancer Center. Other; Modest; PLUS Therapeutics. **J. Floyd:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **E. Galvan:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **M. Hedrick:** A. Employment (full or part-time); Significant; pl. **M. Moore:** A. Employment (full or part-time); Significant; PLUS Therapeutics. **N. LaFrance:** A. Employment (full or part-time); Significant; PLUS Therapeutics.

Abstract Number: 17
Abstract Title: *Assessment of FET PET-based response in patients with gliomas using the PET RANO 1.0 criteria*

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Background:
Recently, the RANO group proposed amino acid PET-based response assessment criteria for diffuse gliomas (PET RANO 1.0). We evaluated these criteria for their predictive value concerning a significantly longer survival in patients with newly diagnosed gliomas undergoing adjuvant temozolomide chemotherapy.
Material and Methods:
We used PET data of an already published study to evaluate the PET RANO 1.0 criteria. In that study, 38 patients (glioblastoma, n=36; H3K27-mutated midline glioma, n=1; astrocytoma CNS WHO grade 4, n=1) after surgery or biopsy and radiotherapy with concomitant temozolomide chemotherapy underwent PET imaging using the radiolabeled amino acid *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (FET) at baseline and after the second cycle of adjuvant temozolomide chemotherapy. We evaluated the predictive value of the PET RANO 1.0 criteria concerning progression-free and overall survival (PFS, OS) using univariate and multivariate survival estimates.
Results:
According to PET RANO 1.0 criteria, patients with a PET-based stable disease (n=22), partial response (n=3), or complete response (n=0) had a significantly longer OS than patients with PET-based progressive disease (n=13) (17.0 vs. 12.0 months; *P*=0.029). In contrast, these criteria could not predict a significantly longer PFS (9.7 vs. 8.1 months; *P*=0.147). Multivariate survival analysis revealed that PET RANO 1.0 criteria changes predicted a significantly prolonged OS independent of age, extent of resection, and O^6-methylguanine-DNA-methyltransferase promoter methylation (*P*=0.002; HR, 4.144; 95% CI, 1.727-10.150).
Conclusion:
Evaluating FET PET changes according to the PET RANO 1.0 criteria seems to identify patients with significantly longer OS but not PFS. The lack of PFS prediction using the PET RANO 1.0 criteria remains unclear and warrants further evaluation of these metabolic response criteria for amino acid PET in patients undergoing brain cancer therapy.

Author Disclosures:
G. Ceccon: None. **M. Wollring:** None. **I. Stetter:** None. **J. Werner:** None. **P. Lohmann:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Blue Earth Diagnostics. **E.K. Rosen:** None. **J. Peplinski:** None. **G.R. Fink:** None. **K. Langen:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Blue Earth Diagnostics. **N. Galldiks:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Blue Earth Diagnostics. F. Consultant/Advisory Board; Modest; Telix.

Abstract Number: 18
Abstract Title: ***Exploring theranostic potential: FAP expression in brain metastases and novel FAPi radiotracers with an alpha-ketoamide warhead***

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Background:
Brain metastases affect approximately 20% of patients with various solid cancers and are the most common malignant tumors of the central nervous system in adults with limited therapeutic options. Fibroblast activation protein (FAP), a serine protease, is expressed in cancer associated fibroblasts (CAF) and cancer cells and represents a promising target for tumor visualization and therapy. The aim of this study was to evaluate FAP expression in brain metastases and to design and test novel FAP targeting compounds (FAPi) utilizing recently developed alpha-ketoamide FAP inhibitors.
Material and Methods:
FAP expression in brain metastases and control non-tumorous brain tissue was determined by an enzymatic assay, ELISA, and immunohistochemistry. Cancer and CAF cell cultures were derived from brain metastases and characterized by imunnocytochemistry. Novel alpha-ketoamide FAPi were labeled with ^{99m}Tc and their binding to FAP-expressing cells was tested.
Results:
FAP expression was significantly higher in BM compared to non-tumorous brain tissue both at the protein and enzymatic activity level. FAP was expressed in CAFs and in addition on tumor cells in a portion of brain metastases. Similar expression pattern was observed in cancer and CAF cultures derived from brain metastases. The ^{99m}Tc-labeled alpha ketoamide FAPi specifically bound to FAP-expressing cells *in vitro*.
Conclusion:
FAP is expressed in brain metastases of diverse solid tumors and represents a potential theranostic target. We are the first to prepare novel FAP radioligands using an alpha ketoamide inhibitor. Ongoing work focuses on establishing suitable *in vivo* brain metastasis models for further development and testing of these compounds. Supported by the project National Institute for Cancer Research (Programme EXCELES, LX22NPO5102) by the EU, Ministry of Health of the Czech Republic, NU22-03-00318, and GA UK no. 342522.

Author Disclosures:
P. Vymola: None. **A. Simkova:** None. **M. Vetrik:** None. **B. Vymolova:** None. **N. Sidej:** None. **J. Kucka:** None. **T. Smetana:** None. **T. Ormsby:** None. **F. Trajhan:** None. **J. Konvalinka:** None. **M. Hruby:** None. **P. Sacha:** None. **A. Sedo:** None. **P. Busek:** None.

Abstract Number: 19
Abstract Title: ***Amino-acid PET as an adjunct to conventional MRI improves the diagnosis of aggressive glial lesions***

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Background:
Amino-acid PET is recommended for the initial diagnosis of brain lesions, but its value for identifying aggressive lesions remains to be established. The current study therefore evaluates the added-value of dynamic ^{18}F-FDOPA PET as an adjunct to conventional MRI for determining the aggressiveness of presumed glial lesions at diagnosis.
Material and Methods:
Consecutive patients, with a minimal 1 year-follow-up, underwent contrast-enhanced MRI (CE_MRI) and dynamic ^{18}F-FDOPA PET to characterize their suspected glial lesion. Lesions were classified semi-automatically by their CE_MRI (MRI-/+), PET (PET-/+) uptake status, and PET parameters (static tumor-to-background ratio, TBR; dynamic time-to-peak ratio, TTP_{ratio}) with thresholds optimized on ROC curves. Aggressive lesions were either defined as lesions with dismal molecular characteristics based on the WHO 2021 classification of brain tumors or with compatible clinico-radiological profiles. Time-to-treatment failure (TTF) and overall survival (OS) were evaluated.
Results:
Of the 109 patients included, 46 had aggressive lesions (45 confirmed by histo-molecular analyses). PET detected 100% of aggressive lesions (vs. 76% sensitivity for CE_MRI). TBR_{max} (threshold of 3.2), and TTP_{ratio} (threshold of 4.8 min) respectively identified aggressive lesions with an accuracy of 79% and 73% and were independent of clinical factors in the multivariate analysis. Among the MRI-lesions, 11/56 (20%) were aggressive and all were PET+. In the MRI+/PET+ group (n=49), a higher TBR_{max} and shorter TTP_{ratio} were associated with poorer survival.
Conclusion:
Dynamic amino-acid PET provides additional information to conventional MRI on the potential aggressive nature of suspected glial lesions at diagnosis, which may be helpful to choose the optimal therapeutic strategy.

Author Disclosures:
A. Zinsz: None. **C. Pouget:** None. **F. Rech:** None. **L. Taillandier:** None. **M. Blonski:** None. **S. Amlal:** None. **L. Imbert:** None. **T. Zaragori:** None. **A. Verger:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Curium, Eisai. F. Consultant/Advisory Board; Modest; General Electrics, Novartis.

Abstract Number: 20
Abstract Title: *Measurable disease for response assessment in IDH-wildtype glioblastoma- a comparison of MRI-based (RANO 2.0) versus PET-based (PET RANO 1.0) assessment*

Authors:
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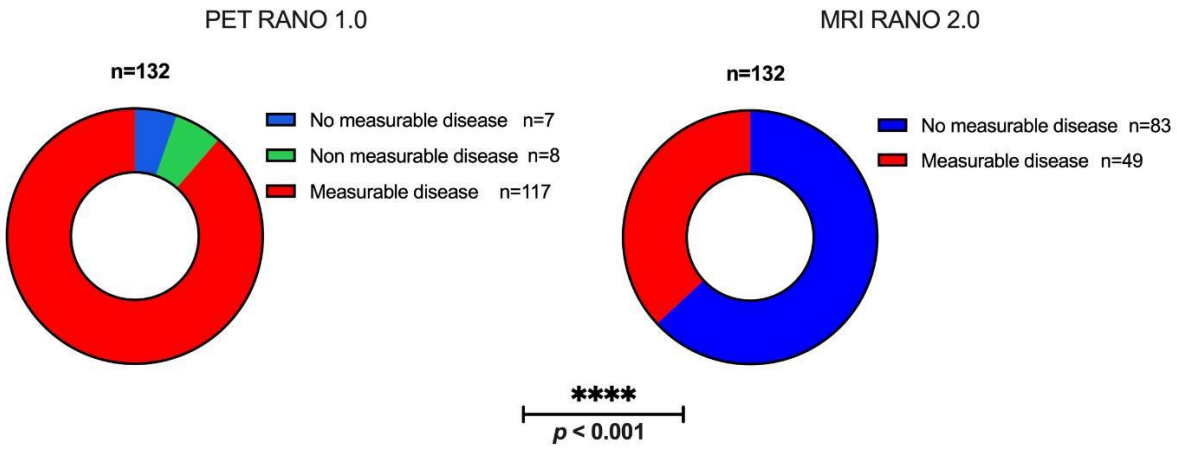
Background:
'Measurable disease' on MRI is the baseline criterion for response assessment in glioblastoma and relies on measuring contrast enhancement. Recently, criteria based on amino acid PET have been proposed for response assessment in clinical trials (PET RANO 1.0 criteria). Here, we compared 'measurable disease' as defined by PET RANO 1.0 criteria with MRI-based RANO 2.0 in patients with IDH-wildtype glioblastoma.
Material and Methods:
In this retrospective single-centre study, patients with newly diagnosed IDH-wildtype glioblastoma with available [^{18}F]FET PET and MRI (median time interval: 5.0 days, IQR:1.0-9.8) prior to or after resection and before chemoradiotherapy were identified (i.e.: baseline timepoint recommended by PET RANO 1.0). Analysis was conducted by two independent investigators to detect 'measurable disease' according to MRI-based RANO 2.0 versus PET-based PET RANO 1.0 criteria as well as lesion size and uptake intensity (maximal, mean target-to-background-ratio: TBR_{max}, TBR_{mean}).
Results:
We evaluated 132 patients (median age 60.5 years, IQR:52.0-70.0; 40.2% females) with 87 cases after biopsy and 45 after resection. Using RANO 2.0, 49/132 (37.1%) patients were classified as having measurable disease (median sum of maximum perpendicular diameters: 36.3mm, IQR: 25.1-49.5mm). However, utilizing PET RANO 1.0, a significantly higher proportion (117/132 88.6%, $p<0.001$) had measurable disease (median TBR_{max}:3.4, IQR:2.5-3.9; median TBR_{mean}: 2.0, IQR:1.8-2.2, median PET volume:17.6cm^3, IQR:8.8-37.9cm^3). Out of the 15 patients without measurable disease on PET, none had measurable disease on MRI. Contrariwise, 68/83 (81.9%) of patients without measurable disease on MRI exhibited measurable disease on PET.
Conclusion:
Using PET RANO 1.0, a significantly higher number of patients with newly diagnosed glioblastoma can be classified as having 'measurable disease' compared to conventional MRI-based criteria in the perioperative period. Therefore, PET-based assessment may serve as a novel baseline parameter in evaluating treatment response and outcome within glioblastoma trials. Further investigation is needed to confirm our results in prospective trials.



Author Disclosures:
K.J. Müller: None. **R. Forbrig:** None. **J. Reis:** None. **L. Wiegand:** None. **E. Barci:** None. **S. Kunte:** None. **L. Kaiser:** None. **N. Thon:** None. **C. Schichor:** None. **P. Harter:** None. **L. von Baumgarten:** None. **M. Preusser:** None. **N. Albert:** None.

Abstract Number: 21
Abstract Title: ***Response of untreated meningioma to Lu-177 DOTATATE: case report and call for further study***

Authors:
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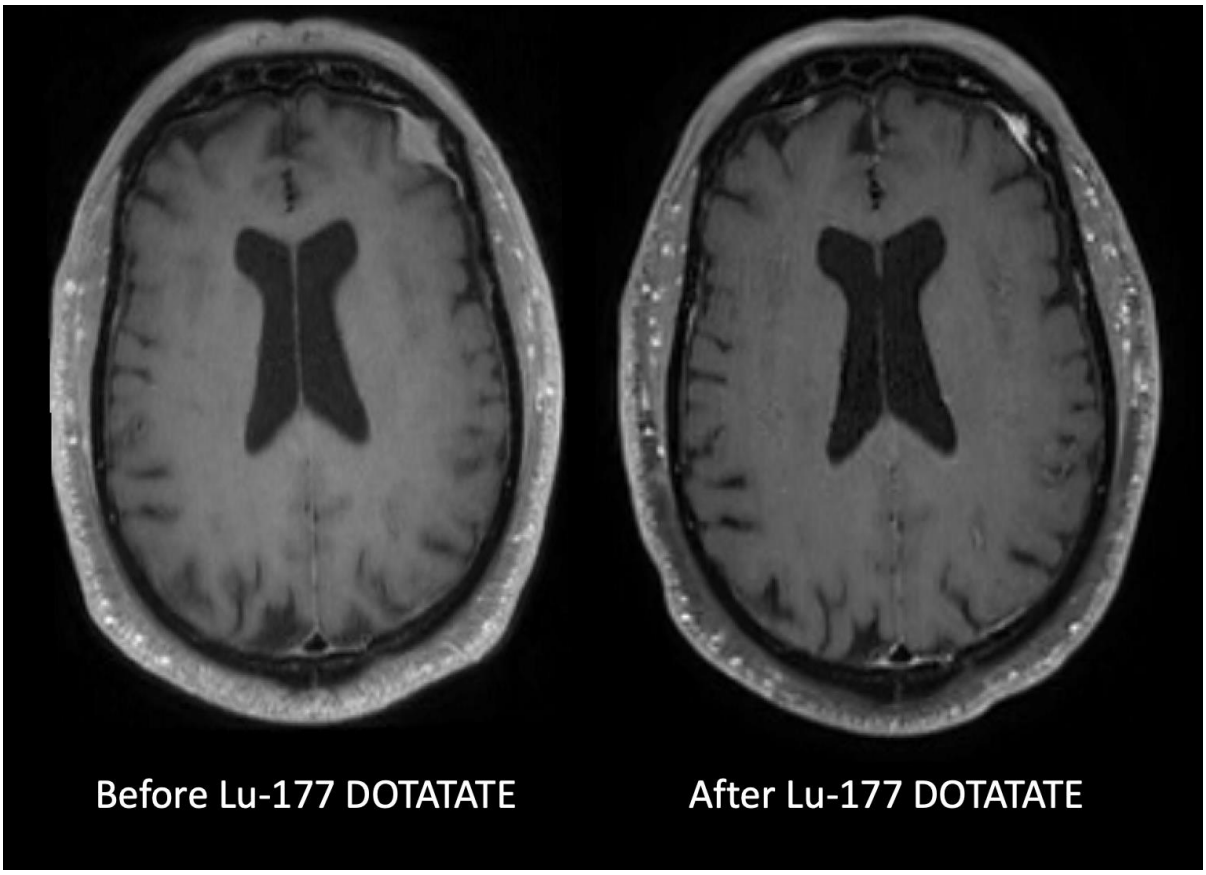
Background:
Lu-177 DOTATATE therapy for meningioma is an area of active research, and may be used off-label treatment for patients with multiply recurrent meningiomas who are not candidates for definitive surgical or external beam radiation treatment. Little is known about the efficacy of Lu-177 DOTATATE for previously untreated meningioma.
Material and methods:
We present a report of objective radiographic response of previously untreated meningioma in a patient who received Lu-177 DOTATATE therapy for another indication.
Results:
An adult patient with metastatic pancreatic neuroendocrine tumor was treated with Lu-177 DOTATATE per standard protocol. The patient had an additional history of incidentally discovered left cerebral convexity meningioma measuring 2.2 by 1.1 cm which had been stable in size over several years. On MR obtained following the fourth cycle of Lu-177 DOTATATE, the meningioma had markedly decreased in size, measuring 0.7 by 0.4 cm. The response has subsequently been maintained for over 3 years without further intervention.
Conclusions:
The literature supporting the use of Lu-177 DOTATATE in meningioma has focused almost exclusively on heavily pretreated patients. Surgery and radiation remain the standard of care for initial therapy of meningioma, but some patients may be poor treatment candidates. This case report demonstrates the potential efficacy of Lu-177 DOTATATE therapy in previously untreated meningioma and suggests that this topic warrants further study.



Author Disclosures:
D.R. Johnson: None. **E. Parent:** None. **J.E. Hammack:** None.

Abstract Number: 22

Abstract Title: ***Update Report of the ReSPECT-GBM Phase 1/2 Dose Escalation Trial of Rhenium (^{186}Re) Obisbemeda (Rhenium-186 Nanoliposome, ^{186}RNL) in Recurrent Glioma via Convection Enhanced Delivery (CED)***

Authors:
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Background:
A Phase 1/2 dose escalation trial was initiated to determine safety and Recommended Phase 2 Dose (RP2D) of a single administration of novel radiotherapeutic ^{186}RNL given by CED for recurrent glioma. ^{186}RNL is nanoliposome-encapsulated rhenium-186, providing locoregional delivery of high-energy beta-particles with simultaneous gamma photon decay for real-time imaging.
Material and Methods:
3+3 modified Fibonacci design was implemented. We report safety and overall survival (OS) in 28 patients over Cohorts 1-8. Patients with biopsy-proven recurrent glioma had placement of up to 5 intracranial catheters to facilitate ^{186}RNL infusion. Whole body planar and SPECT/CT imaging was performed for biodistribution and dosimetry. Patients were followed for safety, dose distribution, progression, and survival.
Results:
Dosing ranged from 1mCi (0.6mL) to 41.5mCi (16.34ml). Maximum-tolerated-dose (MTD) was not reached; no dose-limited-toxicities (DLTs) were observed. Most common adverse events (AEs) were mild (66.7%) or moderate (25.71%) and included headache (6.67%), fatigue (5.24%), muscular weakness (4.29%), seizure (4.29%), and gait disturbance (3.33%); most (85.7%) were unrelated/unlikely-related. Only 8.1% (17) severe AEs were reported; only two were possibly related. Average absorbed dose to the tumor was 264Gy (8.9 Gy to 739.5 Gy). Patients were stratified by absorbed dose (< or ≥100 Gy). In all patients, the median OS (mOS) was 8 months (m) (95%Cl 5m-12m). In those receiving <100Gy, the mOS was 5m (95%Cl 1m-8m) compared to 12m (95% Cl 7m-30m) for those who received ≥100Gy.
Conclusion:
A single administration of ^{186}RNL by CED in recurrent glioma patients is feasible, safe, and potentially effective in increasing overall survival when ≥100Gy radiation is delivered to the tumor. A RP2D of 22.3mCi (8.8mL) was selected for patients with tumors ≤20cm^3. Phase 2 is currently enrolling.

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A. Brenner: A. Employment (full or part-time); Significant; UT Health San Antonio - Mays Cancer Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **A. Bao:** A. Employment (full or part-time); Significant; Case Western Reserve University. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **W. Phillips:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **J. Michalek:** A. Employment (full or part-time); Significant; UT Health San

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Abstract Number: 23

Abstract Title: ***Rhenium (^{186}Re) Obisbemeda (Rhenium-186 Nanoliposome, ^{186}RNL) in Recurrent Glioblastoma (rGBM) via Convection Enhanced Delivery (CED): ReSPECT-GBM Phase 2 Trial Update***

Authors:
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Background:
The Phase 1 ReSPECT-GBM trial (n=28) demonstrated that a single administration of ^{186}RNL by CED in recurrent glioma patients is feasible, safe, and potentially effective in increasing overall survival when ≥100Gy radiation is delivered to the tumor, compared to lower doses and historical controls. A Phase 2 study was initiated with the recommended Phase 2 dose (RP2D); 15 patients at the RP2D have been studied to date.
Material and Methods:
Six Phase 1 patients (Cohort 6) and nine Phase 2 patients were used for data analysis. All received a single dose of 22.3mCi (8.80mL, 2.5mCi/mL) by CED. Eligible participants were ≥18 years of age, able to provide written consent, had histologically confirmed rGBM (1 recurrence), bevacizumab-naïve, and had an enhancing tumor volume within the treatment field volume. All but two patients had tumor volumes ≤20cm^3. Whole body planar and SPECT/CT imaging was performed for biodistribution and dosimetry; longitudinal MRI was performed to assess treatment outcomes. Patients were followed for safety, dose distribution, progression, and survival.
Results:
A single dose of ^{186}RNL was generally safe and well-tolerated, with no dose-limiting-toxicities (DLTs) observed and minimal systemic radiation exposure. No patient had treatment-related adverse events (AEs) with outcome of death, and no patient withdrew due to AEs. Most AEs were mild (66.35%) and moderate (25%) and unrelated/unlikely-related to ^{186}RNL. The average absorbed dose to the tumor was 309.14 Gy (range 62.60-739.5 Gy). mOS was 13 months (m) (95% CI 5m-NA) and median progression free survival (mPFS) was 11m (95% CI 6m-11m) at the time of censoring, tracking consistently with Phase 1 data.
Conclusion:
^{186}RNL therapy resulted in a favorable dose- and volume-dependent impact on mOS without significant toxicity. Phase 2 is ongoing and open to enrollment.

Author Disclosures:
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Modest; PLUS Therapeutics. **J. Michalek:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **J. Floyd:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **S. Huang:** A. Employment (full or part-time); Significant; UT Health San Antonio. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **T. Patel:** A. Employment (full or part-time); Significant; UT Southwestern Medical Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **M. Youssef:** A. Employment (full or part-time); Significant; UT Southwestern Medical Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **J. Weinberg:** A. Employment (full or part-time); Significant; MD Anderson Cancer Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **C. Matsuoka:** A. Employment (full or part-time); Significant; MD Anderson Cancer Center. F. Consultant/Advisory Board; Modest; PLUS Therapeutics. **M. Moore:** A. Employment (full or part-time); Significant; PLUS Therapeutics. **M. Hedrick:** A. Employment (full or part-time); Significant; PLUS Therapeutics. **N. LaFrance:** A. Employment (full or part-time); Significant; PLUS Therapeutics.

Abstract Number: 24
Abstract Title: ***Background region selection in FDOPA PET - comparison of two methods***

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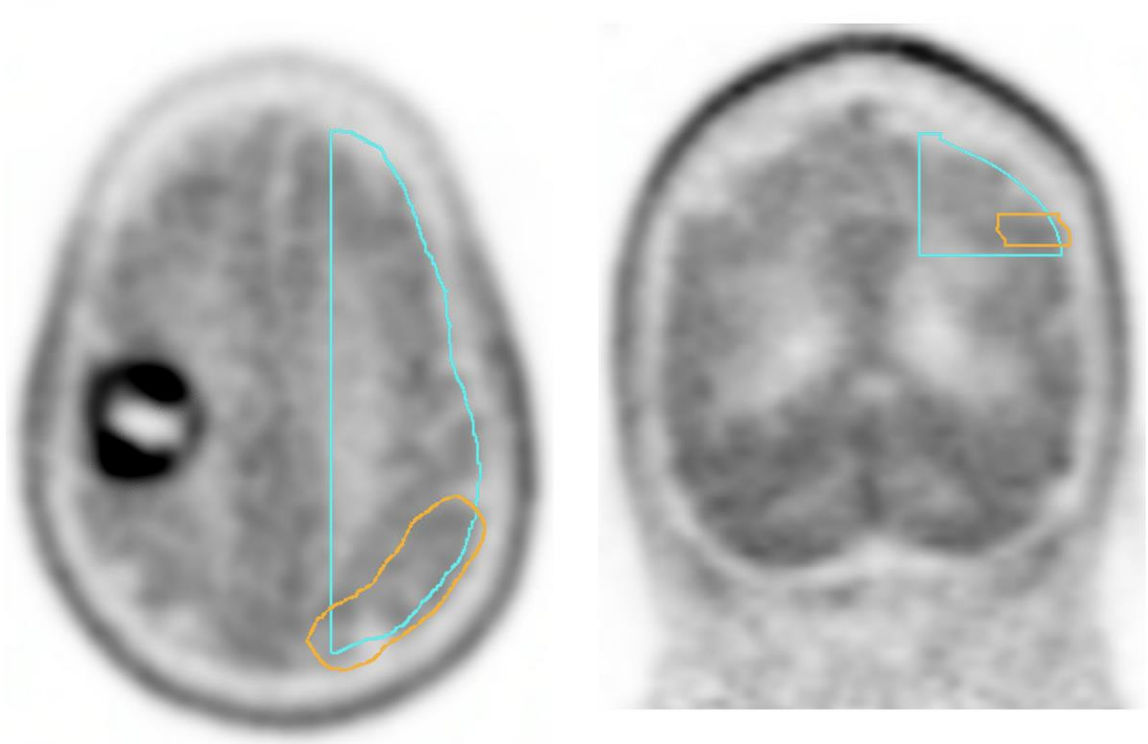
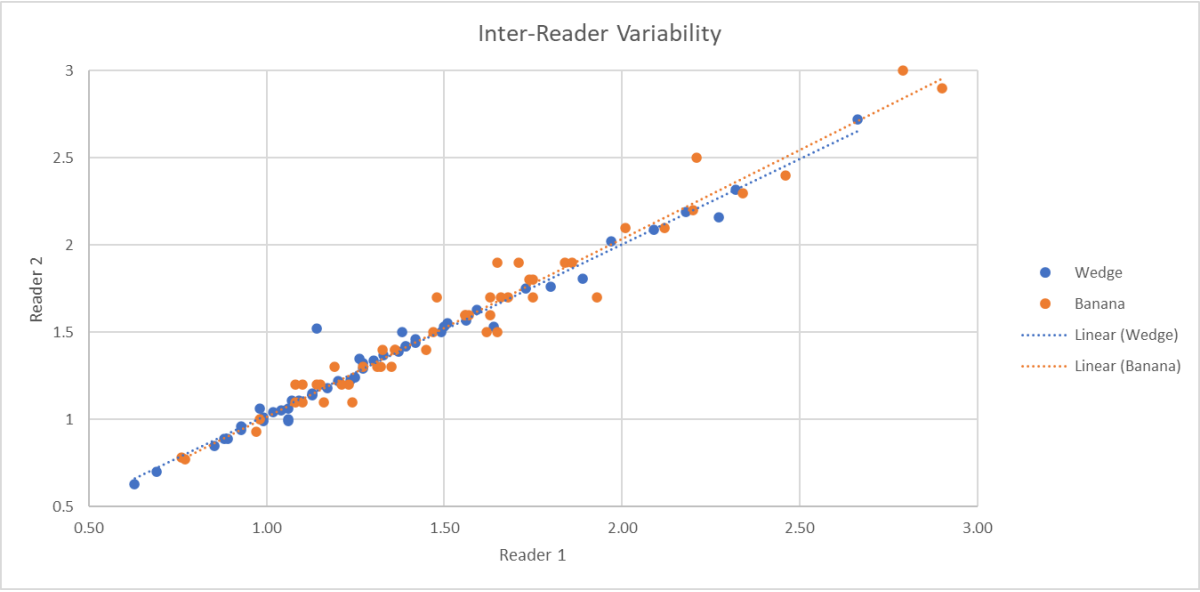
Background:
Quantification of amino acid PET relies on tumor-to-background (TBR) ratios rather than absolute measures of tumor uptake. As such, accurate and reproducible background measurements are vital. While there is robust literature on this topic for FET PET, little has been published for FDOPA.
Materials and Methods:
Two semi-automated methods of FDOPA background region selection were compared by a nuclear medicine radiologist and a medical physicist experienced in amino acid PET imaging. The first method, based on prior institutional experience, created a wedge of brain tissue above the level of the lateral ventricle contralateral to tumor. The second method, based on FET PET literature, created a “banana-shaped” ROI contralateral to the tumor. Agreement between the methods and readers was evaluated.
Results:
FDOPA PET images from 50 patients with newly diagnosed GBM were evaluated. The mean background SUVmean generated by the “wedge” method was 1.37 [95% CI 0.53, 2.20] for reader 1 and 1.35 [95%CI 0.50, 2.19] for reader 2. The mean background SUVmean generated by the “banana” method was 1.58 [95% CI 0.63, 2.53] for reader 1 and 1.55 [95% CI 0.64, 2.46] for reader 2. On a per-patient basis, the mean difference in background SUVmean between the methods was 0.21 [95% CI 0.0, 0.42] for reader 1 and 0.21 [95% CI -0.02, 0.43] for reader 2. Agreement between the readers was slightly greater with the wedge method, with an absolute mean difference of 0.04 compared to 0.07 with the banana method.
Conclusion:
Both methods of background selection were reproducible with minimal inter-reader variability. The wedge method demonstrated mildly but systematically lower background SUVmean values, likely related to inclusion of more white matter and/or CSF spaces within the ROI. Further results, including implications for PET-defined tumor volume, are being evaluated and will be reported at the meeting.



Banana versus Wedge background ROIs



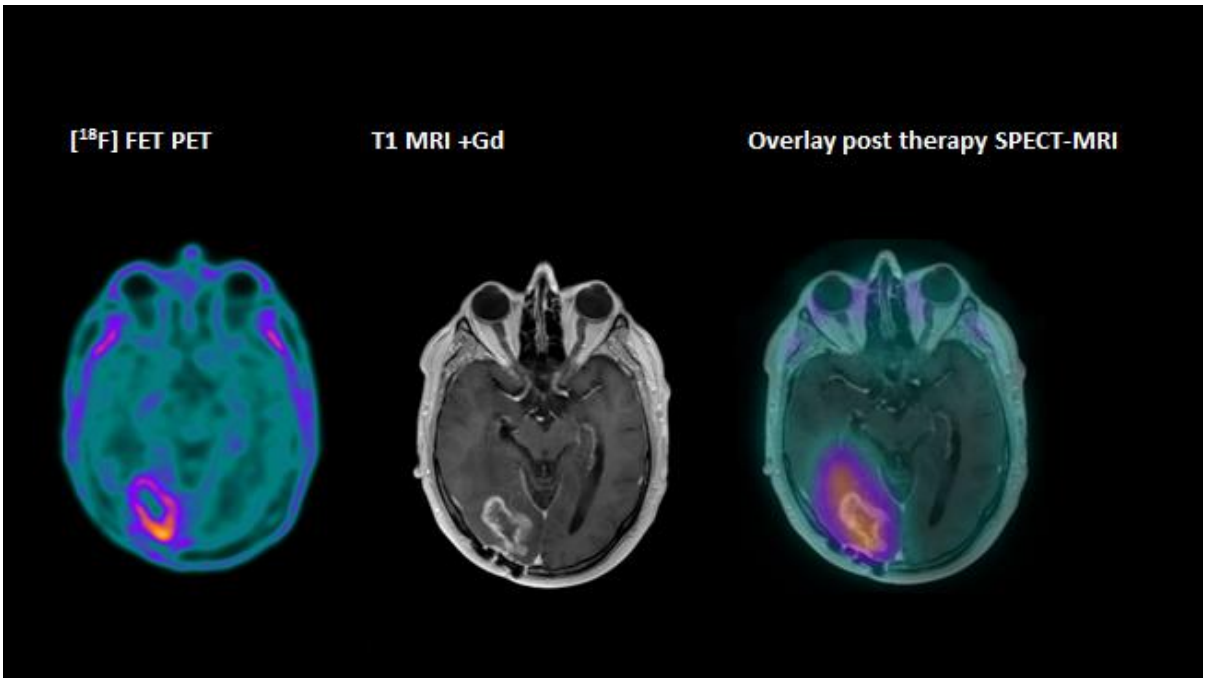
Author Disclosures:
D.R. Johnson: None. **W.G. Breen:** None. **M.P. Thorpe:** None. **D.H. Brinkmann:** None.

Abstract Number: 25

Abstract Title: ***Feasibility and tolerability of [^{131}I]I-PA monotherapy in progressive and recurrent high grade gliomas; a single institution case series.***

Authors:
N. Tolboom[1], T. J. Snijders[1], T. Seute[1], M. Geurts[2], D. Brandsma[3], J. Dankbaar[1], F. Y. De Vos[1], A. J. Braat[1];
[1]University Medical Center Utrecht, Utrecht, Netherlands, [2]Brain Tumor Center at the Erasmus MC Cancer Institute, Rotterdam, Netherlands, [3]Netherlands Cancer Institute, Amsterdam, Netherlands.

Background:
In a phase I-study, safety and tolerability of intravenous 4-L-[^{131}I]iodo-phenylalanine ([^{131}I]I-PA, TLX101, Telix Pharmaceuticals) administered concurrently with second line external beam radiation therapy in patients with recurrent glioblastoma has been demonstrated, with encouraging preliminary efficacy data. Here we report a case series of patients with high grade gliomas treated with [^{131}I]I-PA monotherapy.
Material and Methods:
Patients with 1st or 2nd recurrence of high grade glioma who exhausted local and systemic treatments were referred to our outpatient clinic. Exclusion criteria were life expectancy <12 weeks and KPS >70. [^{18}F]FET-PET was performed, with a minimum tumor-to-background ratio >2,5 being considered adequate for therapy. [^{131}I]I-PA monotherapy was given in an in-patient setting during 3-5 days, depending on emitted radiation levels, in accordance with local radiation safety legislation. Post-therapy SPECT scans were done after three days, clinical follow-up after each cycle, and follow up MRI 3 weeks after the second cycle.
Results:
In August 2021, and between September 2023 and January 2024, five patients (1 oligodendroglioma grade 3, 4 glioblastoma (according to WHO 2021 criteria)) were treated. Mean age was 52±7 years, 5 male. Four patients received two cycles with 5 GBq [^{131}I]I-PA, mean time between treatments was 25 days±4. One patient recently received his first cycle. One second cycle was an experimental intra-arterial administration, all others were intravenous administrations. Treatments were well tolerated, without any treatment-related adverse effects . Adequate targeting was demonstrated visually on post therapy SPECT/CT in all patients. All but one patient (oligodendroglioma treated in august 2021, overall survival ten months) are still alive at time of this interim analysis.
Conclusion:
In this case series of [1^{31}I]I-PA monotherapy in recurrent high-grade gliomas, treatment was feasible and well tolerated. Adequate targeting was revealed at post-therapy SPECT imaging. Efficacy and survival will be evaluated.
Disclosures:
TLX101 provided by Telix Pharmaceuticals

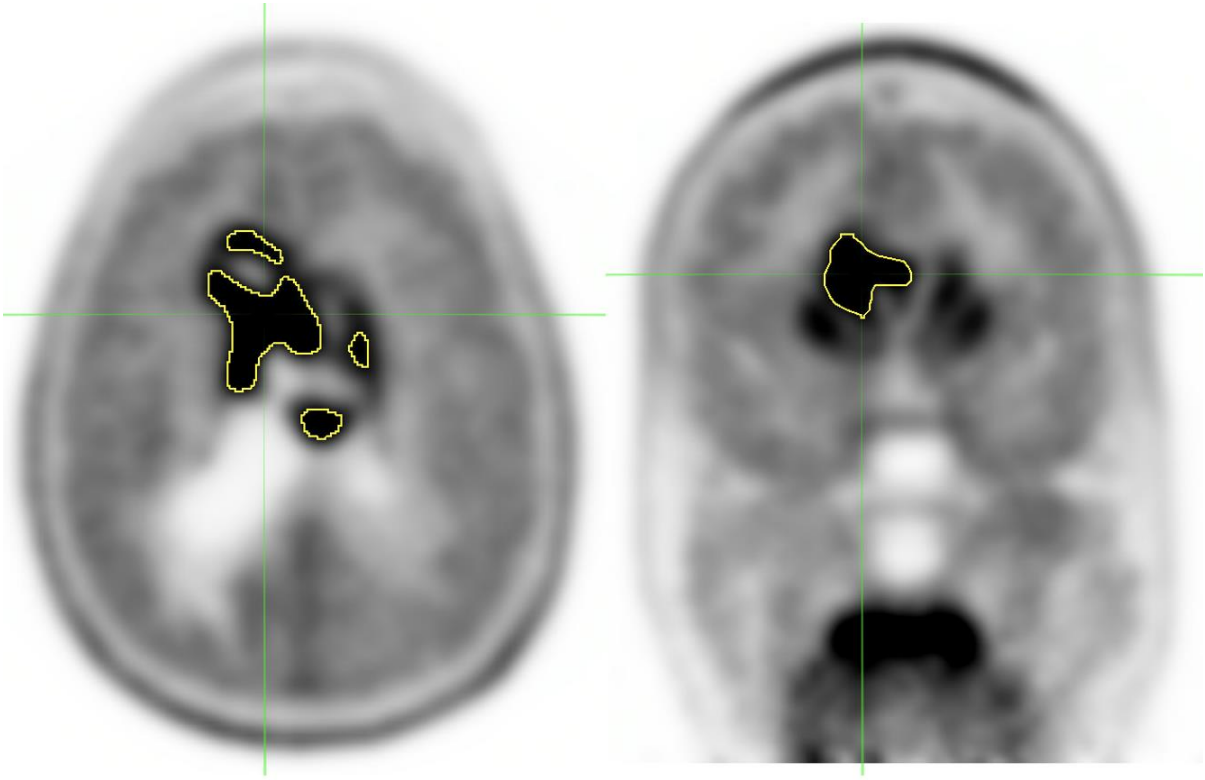


Author Disclosures:
N. Tolboom: None. **T.J. Snijders:** None. **T. Seute:** None. **M. Geurts:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Evgen Pharm. **D. Brandsma:** None. **J. Dankbaar:** None. **F.Y. De Vos:** None. **A.J. Braat:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Ariceum Therapeutics, Rayzebio. F. Consultant/Advisory Board; Modest; Boston Scientific, Terumo, GE Healthcare.

Abstract Number: 26
Abstract Title: ***Physiologic FDOPA uptake in the basal ganglia - implications for tumor delineation in patients with newly diagnosed glioblastoma***

Authors:
D. R. Johnson, W. G. Breen, D. H. Brinkmann;
Mayo Clinic, Rochester, MN, United States.

Background:
Amino acid PET imaging has shown promise as a tool to inform surgical and radiation planning in patients with newly diagnosed glioblastoma. Several amino acid PET agents are used in clinical practice and research, including FDOPA, FET, MET, and flucyclovine, and each has benefits and drawbacks. An often-discussed drawback of FDOPA PET for glioma imaging is physiologic uptake in the basal ganglia, but the real-world frequency with which this interferes with glioblastoma delineation/segmentation is unclear.
Materials and Methods:
As part of an ongoing clinical trial, FDOPA PET/CT was performed for radiation planning in 50 patients with newly diagnosed glioblastoma. PET imaging began 10 minutes after injection of 5.0 (+/- 10%) mCi of FDOPA. Metabolic tumor volumes were segmented based on tumor to background ratios of >=2.1 and >=1.6. Confluence of metabolic tumor with physiologic basal ganglia uptake was evaluated in each patient.
Results:
Fifty patients with GBM were evaluated with FDOPA PET/CT. The TBR>=2.1 volume was continuous with the basal ganglia in 11/50 patients (22%); manual correction to exclude physiologic uptake from the radiation treatment plan was required in these patients. The TBR>=1.6 volume was continuous with the basal ganglia in 21/50 patients (42%).
Conclusion:
Physiological uptake in the basal ganglia remains a pitfall of FDOPA imaging in glioma. While tumor FDOPA uptake does not extend into the basal ganglia in most patients with GBM, a significant minority require manual correction of the PET-defined tumor volume for this reason.



Author Disclosures:
D.R. Johnson: None. **W.G. Breen:** None. **D.H. Brinkmann:** None.

Abstract Number: 27
Abstract Title: ***Predicting intraoperative 5-ALA fluorescence in diffuse low-grade gliomas using preoperative FET-PET***

Authors:
M. Müther, W. Roll, L. König, M. Schäfers, W. Stummer;
University Hospital Münster, Münster, Germany.

Background:
Previous studies have revealed the potential utility of 5-aminolevulinic acid (5-ALA) as a surgical adjunct and prognostication tool in diffuse low-grade gliomas (DLGG). However, besides contrast enhancement, a reliable means of identifying which DLGG will fluoresce has not been established**.** Amino acid PET with [18F]-fluoroethylthyrosine ([^{18}F]FET-PET) can inform delineation of metabolically active tumor components and guide decisions on surgical strategy. This study sheds light on the value of [18F]FET-PET for predicting intraoperative 5-ALA-derived tissue fluorescence.
Material and Methods:
Retrospectively, all therapy-naive patients diagnosed with WHO grade II (WHO CNS 2016) gliomas 2012-2021 were screened for preoperative [18F]FET-PET imaging and 5-ALA fluorescence guided microsurgical resection. All diagnoses were updated for the current 2021 classification of CNS tumors. [18F]FET-PET/CT or PET/MRI were quantitatively analyzed. In cases in which dynamic imaging was available, late uptake kinetics were graded as increasing vs. indifferent/decreasing.
Results:
Information on intraoperative fluorescence was available from 56 patients, of which 36 % presented with positive intraoperative fluorescence**.** Nineteen patients were diagnosed with oligodendroglioma (47% with intraoperative fluorescence) and 36 patients with IDH-mutant astrocytoma (28% with intraoperative fluorescence). Additional 20 patients were diagnosed with a molecular glioblastoma of IDH-wildtype, without imaging or histopathological criteria of malignancy (8% with intraoperative fluorescence). Contingency analyses of neither [18F]FET-PET positivity (P .07, Fisher's exact) nor [18F]FET-PET kinetics (P .99, Fisher's exact) did point on a correlation of [18F]FET-PET and intraoperative 5-ALA-derived fluorescence. In line with previous studies, only gadolinium contrast enhancement is associated with intraoperative fluorescence (P .001).
Conclusion:
Besides being helpful for surgical tumor sampling by depicting tumor heterogeneity, preoperative [18F]FET-PET is of prognostic importance. Same holds true for 5-ALA fluorescence. This study provides indirect evidence, that both methods provide information on tumor heterogeneity in DLGG but do not share a mutual mechanism of action.

Author Disclosures:
M. Müther: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Medac (Wedel, Germany). F. Consultant/Advisory Board; Modest; Medac (Wedel, Germany). **W. Roll:** None. **L. König:** None. **M. Schäfers:** None. **W. Stummer:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Medac (Wedel, Germany), Carl Zeiss Meditech (Oberkochen,

Germany) and NxDc (Lexington, Kentucky). F. Consultant/Advisory Board; Modest; Medac (Wedel, Germany), Carl Zeiss Meditech (Oberkochen, Germany) and NxDc (Lexington, Kentucky).

Abstract Number: 28
Abstract Title: ***11C-Methionin PET for radiotherapy treatment planning in patients with rapid early progression after glioblastoma surgery: prospective phase II trial***

Authors:
T. Kazda[1], R. Lakomy[2], L. Hynkova[1], P. Pospisil[1], J. Vasina[3], R. Belanova[4], T. Prochazka[1], Z. Rehak[3], J. Adam[3], J. Sana[5], I. Selingerova[6], R. Jancalek[7], P. Fadrus[8], K. Polachova[1], M. Budinsky[9], T. Stepankova[10], M. Lojova[10], P. Slampa[1];
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Background:
Radiotherapy (RT) is a standard treatment for nearly all glioblastoma patients following initial surgery. Few retrospective studies indicate negative prognostic instances of progression during the planning magnetic resonance (MR) (up to 1 week before initiating RT), termed Rapid Early Progression (REP). The optimal RT management for REP patients remains uncertain. The objective of this prospective phase II trial (NCT05608395) is to assess impact of 11C-Methionine PET used for RT planning in REP glioblastoma patients.
Material and Methods:
We enrolled glioblastoma, IDHwt, or Astrocytoma, IDHmt, WHO grade IV patients, who developed REP characterized by 1) increase in postoperative residuum by ≥ 25%, 2) appearance of new contras enhancing lesion, 3) unequivocal progression of the unresected satelite. Patients received treatment based on the Stupp or Perry protocol. Treatment response was evaluated using RANO criteria. RT target volumes were delineated as follows: Gross tumor volume included tumor cavity, enhancing lesion and 11C-MET PET (1.3 tumor-to-background ratio). The clinical target volume was GTV plus a modified 2cm margin. The study is designed to demonstrate an increase in progression-free survival (PFS) from 4.9 months (historical cohort with median overall survival (OS) 10.7 months) to a target PFS of 8 months.
Results:
The initial results of the first 26 patients (14 with Stupp protocol), with a median follow-up of 9.7 months, indicate no significant increase in PFS, with a median PFS of 5.6 months (46% at 6 months PFS). However, notable difference between those after Perry protocol (8.5 months) and the Stupp protocol (4.2 months). The median OS 14 months. During the konference updated results will be shown.
Conclusion:

11C-MET PET may be valuable in target definitions for RT of glioblastoma patients with REP. Volumetric studies, patterns of failure and quality of life will be important secondary outcomes. Supported by NU20-03-00148.

Author Disclosures:
T. Kazda: None. **R. Lakomy:** None. **L. Hynkova:** None. **P. Pospisil:** None. **J. Vasina:** None. **R. Belanova:** None. **T. Prochazka:** None. **Z. Rehak:** None. **J. Adam:** None. **J. Sana:** None. **I. Selingerova:** None. **R. Jancalek:** None. **P. Fadrus:** None. **K. Polachova:** None. **M. Budinsky:** None. **T. Stepankova:** None. **M. Lojova:** None. **P. Slampa:** None.

Abstract Number: 29
Abstract Title: ***Investigating the radiobiological response to PRRT using patient-derived meningioma spheroids***

Authors:
T. G. Reuvers[1,2], V. Grandia[3], R. M. Brandt[1], M. Arab[3], S. L. Maas[4,5], J. Nonnekens[1,2], **E. M. Bos**[3,6];
[1]Department of Molecular Genetics, Erasmus MC, Rotterdam, Netherlands, [2]Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, Netherlands, [3]Department of Neurosurgery, Erasmus MC, Rotterdam, Netherlands, [4]Department of Pathology, Erasmus MC, Rotterdam, Netherlands, [5]Department of Pathology, Leiden University Medical Center, Leiden, Netherlands, [6]Erasmus MC Cancer Institute, Rotterdam, Netherlands.

Background:
Peptide receptor radionuclide therapy (PRRT) has recently been evaluated for treatment of meningioma patients. However, current knowledge on the underlying radiation biology is limited, in part due to the lack of relevant *in vitro* models. Here, we developed a meningioma patient-derived 3D culture model to assess the initial response to radiation therapies such as PRRT and external beam radiotherapy (EBRT).
Material and Methods:
Meningioma tissue was cultured as tumor tissue-derived spheroids for 1 week and viability, tumor morphology, histology and expression of tumor-specific markers were compared to parental tumors. Specific binding of PRRT (^{177}Lu-DOTA-TATE) was assessed by uptake assays. DNA damage induced by EBRT and PRRT was assessed by 53BP1 foci quantification.
Results:
We established cultures for 16 meningiomas with high efficiency and yield. In general, meningioma spheroids retained characteristics of the parental tumor during the initial days of culturing. For a subset of tumors, clear changes towards a more aggressive phenotype were visible over time, indicating dedifferentiation induced by the culture method. To assess PRRT efficacy, we demonstrated specific binding of ^{177}Lu-DOTA-TATE to somatostatin receptor subtype 2 (SSTR2), which was highly overexpressed in the majority of tumor samples. PRRT induced DNA damage which was detectable for an extended timeframe as compared to EBRT. Interestingly, levels of DNA damage in spheroids after PRRT correlated with SSTR2-expression levels of parental tumors.
Conclusion:
Our patient-derived meningioma culture model can be used to assess the initial response to PRRT and EBRT in radiobiological studies. Further improvement of this model should pave the way towards development of a relevant culture model for assessment of the long-term response to radiation and, potentially, individual patient responses to PRRT and EBRT.

Author Disclosures:
T.G. Reuvers: None. **V. Grandia:** None. **R.M. Brandt:** None. **M. Arab:** None. **S.L. Maas:** None. **J. Nonnekens:** None. **E.M. Bos:** None.

Abstract Number: 30
Abstract Title: ***Prognostic value of [18F]-FET-PET in diffuse low-grade glioma (Grade 2 WHO CNS 2021)***

Authors:
M. Müther, L. König, M. Schäfers, W. Stummer, W. Roll;
University Hospital Münster, Münster, Germany.

Background:
Amino acid PET with [18F]-fluoroethylthyrosine ([18F]-FET-PET) is frequently used for prognostication and response assessment in treatment of malignant glioma. In diffuse low grade gliomas (DLGG) [18F]-FET-PET can inform delineation of metabolically active tumor components and guide decisions on surgical strategy. This study sheds light on the prognostic value of [18F]FET-PET for therapy-naive patients with DLGG.
Material and Methods:
Retrospectively, all therapy-naive patients with preoperative [18F]FET-PET before microsurgical resection and diagnosed with a WHO grade II lesion (WHO CNS 2016) from 2012-2021 were included in the analysis. Diagnoses were updated according to the 2021 classification of CNS tumors. [18F]FET-PET/CT or PET/MRI were quantitatively analyzed. In cases in which dynamic imaging was available, late uptake kinetics were graded as increasing vs. indifferent/decreasing. Measures were correlated with progression-free survival (PFS).
Results:
Out of 115 patients, 28 (24%) patients were diagnosed with isocitrate dehydrogenase (IDH) mutant and 1q/19q co-deleted oligodendroglioma and 64 (74%) patients with IDH-mutant WHO grade 2 astrocytoma. Twenty-three (26%) patients were diagnosed with IDH-wildtype tumors. Maximum tumor to brain ratio (TBRmax) values are significantly higher in oligodendrogliomas compared to IDH-mutant astrocytomas ($p<0.001$). IDH status does not affect static uptake measures. Increasing late kinetics are associated with longer PFS compared to decreasing/plateau kinetics, only when including IDH-wildtype lesions ($p=0.015$). In the subgroup of IDH-mutant astrocytomas without adjuvant treatment, patients with a TBRmax >1.9 showed significantly shorter PFS compared to patients with lower TBRmax ($p<0.001$).
Conclusion:
Preoperative [18F]FET-PET is not only useful for surgical tumor sampling by depicting tumor heterogeneity, but can also provide prognostic information. Prospective studies need to demonstrate whether [18F]FET-PET can be used as decision support to vote for or against adjuvant therapies after microsurgical resection.

Author Disclosures:
M. Müther: None. **L. König:** None. **M. Schäfers:** None. **W. Stummer:** None. **W. Roll:** None.

Abstract Number: 31
Abstract Title: ***68Ga-DOTATATE PET-CT in treatment planning of robotic stereotactic CyberKnife radiation therapy in patients with intracranial meningiomas***

Authors:
H. Grzbiela, E. Nowicka, E. Staniewska, M. Stapor-Fudzinska, R. Tarnawski;
Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland.

Background:
The aim of this study was to analyze the impact of implementation of 68Ga-DOTATATE PET-CT on the precision of radiotherapy planning for meningiomas, considering the fact that meningioma cells express somatostatin receptors.
Material and Methods:
We analyzed a group of 35 patients (24 women and 11 men), aged 40-78 years (median age 62 years), diagnosed with intracranial meningiomas. Before showing up at our hospital, due to tumor location or rapid progression, fifteen patients underwent surgery as primary treatment. Twenty patients had no previous surgery. Tumor location was skull base (25 patients), parafalx region (2 patients), cerebral convexity (4 patients), optic nerve sheath (1 patient) and other locations (3 patients). All patients were qualified for radiotherapy. To ensure best tumor visualization not only CT and MRI scans, but also 68-Ga-DOTATATE-PET-CT scans were obtained. Maximal SUV values in PET scans ranged from 3.27 to 53.49.
Results:
All images (CT, MRI, and 68-Ga-DOTATATE-PET-CT) were imported into CyberKnife MultiPlan System. Gross tumor volume (GTV) was delineated twice: using MRI/CT fusion (GTV1) and PET/CT fusion (GTV2). In thirteen patients GTV2 was larger than GTV1, those were patients with skull base meningiomas and all of them underwent previous neurosurgery. Planning target volume included a sum of GTV1 and GTV2 and ranged from 9.8 cm^3 to 27.2 cm^3 (mean 19.8 cm^3). This analysis shows that the integrated data of MRI/PET/CT scans can result in improved target delineation. All patients were given total dose of 18 Gy in 3 fractions using robotic CyberKnife radiotherapy. Local control was achieved in 33 patients. Two patients showed progressive disease 12 and 41 months after radiotherapy.
Conclusion:
68-Ga-DOTATATE-PET-CT is a valuable tool in radiotherapy treatment planning process. It defines more clearly gross tumor volume (compared to usual CT/MRI fusion), especially for meningiomas after subtotal resection and those located at skull base.

Author Disclosures:
H. Grzbiela: None. **E. Nowicka:** None. **E. Staniewska:** None. **M. Stapor-Fudzinska:** None. **R. Tarnawski:** None.

Abstract Number: 32
Abstract Title: ***Fractionated intracavitary radioimmunotherapy with Lu-177 labeled 6A10 Fab fragments in patients with malignant glioma: a phase I trial to determine maximum tolerated dose and toxicity***

Authors:
M. Müther[1], W. Roll[1], G. Böning[2], A. Delker[2], N. Warneke[1], F. Gildehaus[2], M. Schäfers[1], L. Stegger[1], W. Stummer[1], H. Reulen[2];
[1]University Hospital Münster, Münster, Germany, [2]University Hospital LMU Munich, Munich, Germany.

Background:
After completion of first-line treatment, approved maintenance therapies for malignant glioma are lacking. In line with the infiltrative biology of diffuse gliomas, most disease recurrences occur around the resection cavity. Adjuvant intracavitary radio-immunotherapy (iRIT) applied into the resection cavity, offers a promising strategy to address this hibernating tumor burden.
Material and Methods:
LuCaFab (Lu-177 labeled 6A10- Fab-fragment) is a carbonic anhydrase XII-specific antibody Fab fragment labeled with radioisotope lutetium-177. Patients with malignant glioma after surgical cytoreduction, radiochemotherapy and adjuvant chemotherapy are eligible for study participation. Patients will receive the calculated total doses of Lu-177-labeled 6A10-Fabs in three fractions with an interval of 4 weeks between injections, administered into the tumor cavity via an implanted reservoir. A patient specific dosing strategy will be applied.
Results:
This investigator-initiated trial (NOA-22 study, NCT05533242) in a 3x3 dose escalation design is sponsored by the University Hospital Münster. Four study sites (University Hospitals Münster, Essen, Cologne, and Würzburg) are recruiting. The first patient was included in January 2024.
Conclusion:
This is the first prospective multicenter study on iRIT for malignant glioma. Based on experiences with compassionate use cases before study initiation, radioimmunotherapy with Lu-177 labeled 6A10-Fab fragments appears to be a safe maintenance therapy. The NOA-22 study is open for recruitment in four German centers.

Author Disclosures:
M. Müther: None. **W. Roll:** None. **G. Böning:** None. **A. Delker:** None. **N. Warneke:** None. **F. Gildehaus:** None. **M. Schäfers:** None. **L. Stegger:** None. **W. Stummer:** None. **H. Reulen:** None.

Abstract Number: 33
Abstract Title: ***FET-PET-Guided management of pseudoprogression in glioblastoma (the FET POPPING trial): protocol for a diagnostic randomized clinical trial***

Authors:
V. Ruijters[1], T. Snijders[1], M. Geurts[2], E. van de Giessen[3], M. Broen[4], M. Anten[4], A. Arens[5], D. Henssen[5], A. Gijtenbeek[5], M. van der Meulen[6], M. Vos[7], I. Bosma[8], G. Stormezand[8], G. Frederix[1], R. ten Ham[1], J. Dankbaar[1], P. Robe[1], J. Verhoeff[3], F. de Vos[1], N. Tolboom[1];
[1]UMC Utrecht, Utrecht, Netherlands, [2]Erasmus MC, Rotterdam, Netherlands, [3]Amsterdam UMC, Amsterdam, Netherlands, [4]Maastricht UMC, Maastricht, Netherlands, [5]Radboud UMC, Nijmegen, Netherlands, [6]Medisch Spectrum Twente, Enschede, Netherlands, [7]Haaglanden MC, The Hague, Netherlands, [8]UMC Groningen, Groningen, Netherlands.

Background
During follow-up of glioblastoma patients after chemoradiation, expert teams often observe MRI abnormalities with difficulty in distinguishing between tumor growth and pseudoprogression. Although techniques such as perfusion MRI provide additional information, diagnostic uncertainty often remains, leading to incorrect or delayed diagnosis and inappropriate treatment, such as unnecessary surgery. Despite the good discriminating power of [^{18}F] FET-PET, this diagnostic tool is not used frequently in the Netherlands due to costs, logistics, and misconceptions about clinical benefit. In the FET-POPPING study we aim to determine the added value of [^{18}F] FET-PET for clinical management.
Material and Methods
A multicenter diagnostic randomized clinical trial will be performed, from July 2024 untill December 2027. 144 adult patients with IDH-wildtype glioblastoma will be included, who, after the concomitant phase of chemoradiation, have increased contrast enhancement on MRI, causing doubt between tumor growth or pseudoprogression. Included patients will be randomized 1:1 in two arms. The investigational arm receives an additional [^{18}F] FET-PET scan, and clinical management is based on the index MRI and [^{18}F] FET-PET together. Clinical management of the control arm is based on the index MRI alone. Exact clinical management, following from the available imaging, is chosen at the discretion of a multidisciplinary board. The primary study endpoints are (a) the percentage of patients undergoing unnecessary interventions and (b) health-related quality of life after 12 weeks. Secondary endpoints include time-to-diagnosis, overall survival and cost-effectiveness.
Expected results
We hypothesize that the clinical management guided by an additional [^{18}F] FET-PET scan leads to fewer unnecessary interventions and, better health-related quality of life after 12 weeks with favorable effects on secondary endpoints, compared with management based on MRI alone.

Author Disclosures:
V. Ruijters: None. **T. Snijders:** None. **M. Geurts:** None. **E. van de Giessen:** None. **M. Broen:** None. **M. Anten:** None. **A. Arens:** None. **D. Henssen:** None. **A. Gijtenbeek:** None. **M. van der Meulen:** None. **M. Vos:** None. **I. Bosma:** None. **G. Stormezand:** None. **G. Frederix:** None. **R. ten Ham:** None. **J. Dankbaar:** None. **P. Robe:** None. **J. Verhoeff:** None. **F. de Vos:** None. **N. Tolboom:** None.

Abstract Number: 34

Abstract Title: ***Somatostatin receptor subtype expression and radiomics from DWI-MRI represent SUV of [68Ga]Ga-DOTATOC PET in patients with meningioma***

Authors:
S. Iglseder[1], A. Iglseder[2], V. Beliveau[1], J. Heugenhauser[1], E. R. Gizewski[3], J. Kerschbaumer[4], G. Stockhammer[1], C. Uprimny[5], I. Virgolini[5], J. Dudas[6], M. Nevinny-Stickel[7], C. Scherfler[1], **M. Nowosielski**[1]; [1]Medical University Innsbruck, Department of Neurology, Innsbruck, Austria, [2]Department of Geodesy and Geoinformation, Technical University Vienna, Vienna, Austria., Vienna, Austria, [3]Medical University Innsbruck, Department of Neuroradiology, Innsbruck, Austria, [4]Medical University Innsbruck, Department of Neurosurgery, Innsbruck, Austria, [5]Medical University Innsbruck, Department of Nuclear Medicine, Innsbruck, Austria, [6]Department of Otorhinolaryngology, Innsbruck Medical University, Innsbruck, Austria., Innsbruck, Austria, [7]Medical University Innsbruck, Department of Radiationoncology, Innsbruck, Austria.

Background:
This retrospective study aimed to analyse the correlation between somatostatin receptor subtypes (SSTR 1-5) and maximum standardized uptake value (SUVmax) in meningioma patients using Gallium-68 DOTA-D-Phe1-Tyr3-octreotide Positron Emission Tomography ([68Ga]Ga-DOTATOC PET). Secondly, we developed a radiomic model based on apparent diffusion coefficient (ADC) maps derived from diffusion weighted magnetic resonance images (DWI MRI) to reproduce SUVmax.
Material and Methods:
The study included 51 patients who underwent MRI and [68Ga]Ga-DOTATOC PET before meningioma surgery. SUV_{max} values were quantified from PET images and tumour areas were segmented on post-contrast T1-weighted MRI and mapped to ADC maps. A total of 1940 radiomic features were extracted from the tumour area on each ADC map. A random forest regression model was trained to predict SUV_{max} and the model's performance was evaluated using repeated nested cross-validation. The expression of SSTR subtypes was quantified in 18 surgical specimens and compared to SUV_{max} values.
Results:
The random forest regression model successfully predicted SUV_{max} values with a significant correlation observed in all 100 repeats ($p < 0.05$). The mean Pearson's r was 0.42 ± 0.07 SD, and the root mean square error (RMSE) was 28.46 ± 0.16. SSTR subtypes 2A, 2B, and 5 showed significant correlations with SUV_{max} values ($p < 0.001$, $R2 = 0.669$; $p = 0.001$, $R2 = 0.393$; and $p = 0.012$, $R2 = 0.235$, respectively).
Conclusion:
SSTR subtypes 2A, 2B, and 5 correlated significantly with SUVmax in meningioma patients. The developed radiomic model based on ADC maps effectively reproduces SUVmax using [68Ga]Ga-DOTATOC PET.

Author Disclosures:
S. Iglseder: None. **A. Iglseder:** None. **V. Beliveau:** None. **J. Heugenhauser:** None. **E.R. Gizewski:** None. **J. Kerschbaumer:** None. **G. Stockhammer:** None. **C. Uprimny:** None. **I. Virgolini:** None. **J. Dudas:** None. **M. Nevinny-Stickel:** None. **C. Scherfler:** None. **M. Nowosielski:** None.

Abstract Number: 35
Abstract Title: ***Role of FET-PET-based re-irradiation in recurrent glioblastoma - results of a prospective randomized clinical trial***

Authors:
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Background:
This trial aimed to assess the role of O-(2-[18F]fluoroethyl)-L-tyrosine (FET)-positron emission tomography (PET) compared to contrast-enhanced T1-weighted magnetic resonance imaging (T1Gd-MRI) for re-irradiation target volume delineation in recurrent glioblastoma (rGBM).
Material and Methods:
We conducted a prospective, multicenter trial (NOA 10/ARO 2013-1, DKTK-a.) that randomized patients with rGBM 1:1 between FET-PET-based and T1Gd-MRI-based target volume delineation. Patients received high-precision stereotactic re-irradiation with 39 Gy à 3 Gy, 5x/week. The primary endpoint was progression-free

survival (PFS) from randomization, and secondary endpoints included overall survival (OS), locally controlled survival (LCS), and toxicity.

Results:

From 11/2013 to 09/2021, 200 patients were randomized between FET-PET- (n=100) and GdT1-MRI-based (n=100) target volume delineation (n=98 and n=97 per protocol). Median PFS was 4.0 months (95% confidence interval [CI] 3.7-5.2) in the FET-PET arm and 4.9 months (95% CI 3.7-6.0) in the GdT1-MRT arm (one-sided stratified log-rank test p=0.98; adjusted HR for the experimental versus the control arm 1.14 [95% CI 0.85-1.52], p=0.39;). Median OS was 9.4 months (95% CI 7.8-11.1) in the FET-PET arm and 9.0 months (95% CI 7.6-10.5) in the GdT1-MRI arm (HR 1.01 [95% CI 0.75-1.37], p=0.92). Median LCS was 6.3 months (95% CI 5.1-7.2) in the FET-PET arm and 6.8 months (95% CI 6.2-7.3) in the GdT1-MRI arm (HR 1.20 [95% CI 0.88-1.62], p=0.25). Out of 239 patients who received the FET tracer, 9 reported 13 adverse events and 3 reported 5 SAEs in the timespan of 7 days after FET-PET. No event was related to the application of the FET tracer.

Conclusion:

The trial did not demonstrate a benefit of FET-PET-based re-irradiation over GdT1-MRI-based treatment in patients with recurrent glioblastoma (rGBM). The FET-PET examination was well-tolerated in all cases. As the trial exclusively included PET-positive patients, its findings do not impact the diagnostic role of FET-PET in recurrent gliomas.

Author Disclosures:

A.L. Grosu: None. **W.A. Weber:** None. **E. Graf:** None. **M. Mix:** None. **R. Wiehle:** None. **U. Nestle:** None. **M. Niyazi:** None. **C. Belka:** None. **F. Paulsen:** None. **M.J. Eble:** None. **F.A. Giordano:** None. **F. Momm:** None. **S.E. Combs:** None. **R. Engenhart-Cabillic:** None. **M. Stuschke:** None. **R. Fietkau:** None. **T. Brunner:** None. **S. Nadji:** None. **B.J. Krause:** None. **B.G. Baumert:** None. **C. Nieder:** None. **J. Beck:** None. **P.T. Meyer:** None. **H. Urbach:** None. **I. Popp:** None.

Abstract Number: 36
Abstract Title: ***^{177}Lu-PSMA radioligand therapy in patients with brain metastases from prostate cancer: the Innsbruck experience.***

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Background:
The efficacy of PSMA-targeted radioligand therapy (RLT) for brain metastases from castration-resistant prostate cancer (PCa) remains to be determined, as these patients are extremely rare (0.3%-2.8% of patients with PCa) and were generally excluded from major clinical trials.
Material and Methods:
A retrospective review of the medical records of patients who underwent ^{177}Lu-PSMA-617(*) or ^{177}Lu-PSMA-I&T(†) RLT at the Medical University of Innsbruck was performed in order to search for patients with brain metastases.
Results:
Of 178 patients treated between 2015 and 2022, four (2,2%) presented with a total of 6 brain metastases from castration-resistant PCa at the time of RLT. The characteristics of these patients are summarized in Table 1. ^{68}Ga-PSMA-11 uptake of brain metastases prior to RLT was high in patients #1, #2 and #4 (SUVmax>16, >20 and >14, respectively), whereas it was low (SUVmax = 1.1) in patient #3. ^{68}Ga-PSMA-11 brain PET performed two months after completion of RLT was unremarkable in patient #1 and #2, suggesting complete response of all lesions (See Figure 1). These patients died 8 and 5 months after RLT, respectively, due to extracranial progression (no intracranial progression). Post-therapy ^{68}Ga-PSMA-11 PET showed intracranial progression in patient #3, who was later referred for whole-brain radiotherapy. The patient died 27 months after the end of RLT. Post-therapy scan after the fourth RLT cycle showed a stable intracranial disease in patient #4. The patient was subsequently lost at follow-up.
Conclusion:
Brain metastases from castration-resistant PCa may show variable responses to ^{177}Lu-PSMA-617, possibly depending on baseline PSMA PET uptake. Larger series are needed to assess the efficacy of ^{177}Lu-PSMA-617 in brain metastases. Prospective collection of dosimetric data may help establish dose/response correlations and inform combination treatments with external beam radiotherapy.

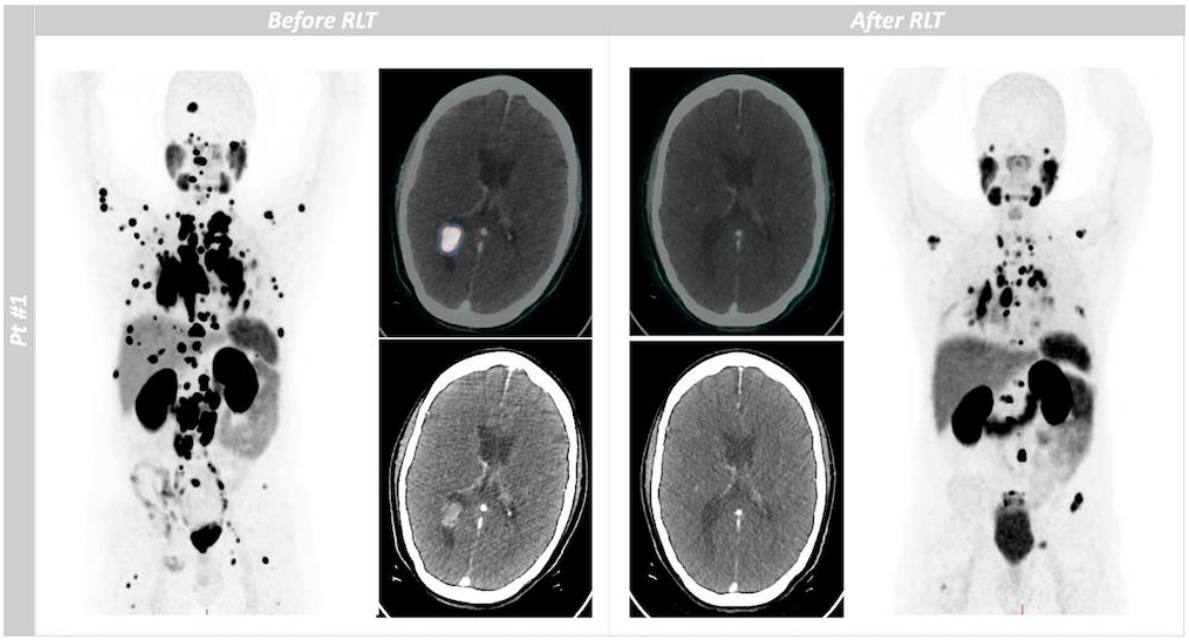

Table 1. Patients' characteristics

Patient	Age	Gleason Score	Baseline PSA (ng/ml)	N° of CNS mets	^{68}Ga-PSMA uptake of CNS mets (SUVmax)	N° of therapy cycles	Total administered activity (GBq)	End of treatment PSA (ng/ml)	Local response
#1	66	9	95,66	1	16,3	6†	43,9	5,43	CR
#2	81	10	482,0	2	20,8	4*	24,3	92,0	CR
#3	63	8	4,66	2	1,1	6*	36,2	17,1	PD
#4	72	7	133,0	1	14,4	4†	30,5	99,7	SD

Author Disclosures:
G. Santo: None. **G. Di Santo:** None. **F. Cicone:** None. **I. Virgolini:** None.

Abstract Number: 37
Abstract Title: *Hybrid [18F]FET PET-MRI; a valuable advanced imaging tool to discriminate between progression of disease and treatment-related changes in glioma patients*

Authors:
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Erasmus MC, Rotterdam, Netherlands.

Background:
Although the clinical importance of MRI in the response assessment of glioma is undisputed, there are known limitations for differentiation between progression of disease (POD) and treatment-related changes (TRC). Hybrid PET-MRI using the tracer O-(2-18F-fluoroethyl)-L-tyrosine ([18F]FET) can potentially aid in the differentiation between POD and TRC by providing concurrent anatomical, functional and metabolic (i.e. amino acid metabolism) information. We evaluated our first series of patients scanned because of equivocal findings on MRI-only.
Material and Methods:
All patients who underwent hybrid [18F]FET PET-MRI in the academic Erasmus medical centre and who had a post-imaging follow-up time of at least 3 months were included. Patients received a 45 minute combined static and dynamic [18F]FET PET-MRI-scan including diffusion weighted imaging (DWI), perfusion weighted imaging (PWI) and post-gadolinium sequences. Outcomes of hybrid imaging reports were compared to previously-obtained MRI, post-operative pathology, and clinical/radiological follow-up.
Results:
Twenty patients with either low-grade (13/20) or high-grade (7/20) glioma were included. All patients received surgery and/or radiotherapy with a median interval time of 31 months (range: 13-96 months) prior to inclusion. [18F]FET PET-MRI was positive, i.e. suggestive for POD, in 15/20 patients (75%). This was confirmed progression in all cases by either pathology (n=7/15) or clinical and radiological follow-up (n=8/15), with a mean follow-up time of 9 months (range: 3-17 months). Five out of 20 patients (25%) had a negative [18F]FET PET-MRI suggestive for TRC. In follow-up none of the patients showed clinical or radiological signs of POD after an average follow-up time of 13 months (range: 11-20 months).
Conclusion:
Hybrid [18F]FET PET-MRI showed high accuracy for the detection of POD in our retrospective cohort of glioma patients with equivocal findings on MRI-only. This novel state-of-the-art imaging technique therewith provided a valuable contribution to follow-up and clinical decision-making.

Author Disclosures:
J. de Jong: None. **I.J. Pruis:** None. **A.A. Harteveld:** None. **M. Segbers:** None. **R. Valkema:** None. **M. Geurts:** None. **F.A. Verburg:** None. **M.J. van den Bent:** None. **S.E. Veldhuijzen van Zanten:** None.

Abstract Number: 38
Abstract Title: *Fostering clinical translation of artificial intelligence in neuro-oncology - establishing an infrastructure for multi-centric data collection, exchange, and analysis*

Authors:
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Background:
Despite the increasing body of literature highlighting the added value of AI methodologies in neuro-oncology, the successful translation into clinical practice remains scarce. This discrepancy results not only from regulatory and data protection hurdles but also from the limited availability of multi-center datasets. To facilitate the clinical translation of AI and its potential to attract investment from industry, AI techniques need to be integrated in prospective clinical trials. To this end, an infrastructure enabling the Europe-wide exchange of neuroimages, and clinical data is needed.
Material and Methods:
The successful deployment of such an infrastructure for this Europe-wide initiative requires participation of sites with an outstanding technical infrastructure and a high level of expertise in implementing legal and data protection regulations. Sites that offer an infrastructure including high-performance computers with many years of experience in both the implementation of EU-wide infrastructure projects as well as storage and exchange of sensitive data seem particularly suitable. One example is the Juelich Supercomputing Center in Germany, which, as one of the leading partners in the Human Brain Project, successfully implemented such an infrastructure in the past.
Results:
Following the evaluation of sites for eligibility, the implementation of an automated process with initial pre-processing including pseudonymization of neuroimaging and clinical data during data upload is planned. Subsequently, this process and the data accessibility will be carefully evaluated with the help of national institutions prior to extension to other European sites.
Conclusion:
Such infrastructure has the potential to significantly advance the development and clinical translation of AI technologies to improve the management of patients with brain tumors. Enabling access to large, curated multi-centric datasets for model testing and development as well as the integration of neuroimaging and clinical data into prospective clinical trials has the potential to facilitate the clinical translation of AI techniques.

Author Disclosures:

P. Lohmann: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Blue Earth Diagnostics. **N. Galldiks:** D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Blue Earth Diagnostics. F. Consultant/Advisory Board; Modest; Telix Pharmaceuticals. **S. Diaz:** None. **N.J. Shah:** None. **F.M. Mottaghy:** None. **K. Langen:** F. Consultant/Advisory Board; Modest; Telix Pharmaceuticals. **M. Preusser:** F. Consultant/Advisory Board; Modest; Bayer, Bristol-Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMC Contrast, GlaxoSmithKline, Mundipharma, Roche, BMJ Journals, MedMedia, Astra Zeneca, AbbVie, Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dome, Tocagen, Adastra, Gan & Lee Pharmaceuticals, Servier, Miltenyi, Telix Pharmaceuticals, Böhringer-Ingelheim, Medscape. **N.L. Albert:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Novocure. F. Consultant/Advisory Board; Modest; Novartis/Advanced Accelerator Applications, Telix Pharmaceuticals, Servier.

Abstract Number: 39
Abstract Title: *Fibroblast activating protein (FAP) expression as potential theranostics target in high-grade meningioma*

Authors:
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Background:
Meningiomas are the most frequent primary neoplasms in the brain and generally cured by resection. However, higher-grade tumors show elevated recurrence rates, underscoring the need for further treatment modalities in addition to standard radiotherapy. “Theranostics” approaches linking tumor-specific antibodies or ligands with radionuclides combine the diagnostic value of functional imaging with the therapeutic activity of radioactive compounds.
Material and Methods:
Patients with histologically verified atypical (WHO grade 2) or anaplastic (WHO grade 3) meningioma were included. Expression of fibroblast activating protein (FAP) as potential treatment target was assessed by immunohistochemistry using anti-FAP antibody (clone JA56-11). Whole-genome DNA methylation profiles were analyzed using Illumina EPIC methylation arrays, and panel sequencing for *NF2, PIK3CA, SMO, ARID1A, ARID1B, KLF4, SUFU, TRAF7*, and the *TERT* promotor was performed using the Illumina NextSeq 500 platform.
Results:
59 patients with a median age of 60 years (range: 19-83) were included, of whom 35 (59.3%) were female. Overall, 40/59 (67.8%) tumors were classified as WHO grade 2 and 19/59 (32.2%) as WHO grade 3. Prognostic DNA methylation classes (MC) were benign-1 (ben-1) in 10 (16.9%), ben-2 in 9 (15.3%), ben-3 in 4 (6.8%), intermediate-A in 23 (40.0%), intermediate-B in 4 (6.8%), and malignant in 9 (15.3%) tumors. FAP expression was observed in 15/59 (25.4%) samples and was significantly associated with WHO grade (WHO grade 2: 2/40, 5.0% vs. WHO grade 3: 13/19, 68.4%; $p<0.001$, Fisher’s exact test). In line, 2 of 4 (50.0%) meningiomas with MC intermediate-B were FAP+, followed by 4/9 (44.4%) with MC malignant, 4/10 (40%) with MC ben-1, and 5/18 (27.8%) with MC intermediate-A ($p=0.092$). FAP+ tumors more frequently showed mutations in NF2 (10/15, 66.7%) than their negative counterparts ($p=0.037$).
Conclusion:
FAP may represent a promising target for theranostics approaches in meningioma, especially in those with malignant biological behavior.

Author Disclosures:

M.J. Mair: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Bristol-Myers Squibb. Other; Modest; Pierre Fabre. **S. Hartenbach:** None. **E. Tomasich:** None. **G. Widhalm:** None. **F. Eckert:** F. Consultant/Advisory Board; Modest; Servier, Dr. Sennewald Medizintechnik. **F. Sahm:** E. Ownership Interest (stock, stock options, patent or other intellectual property); Modest; Heidelberg Epignostix GmbH. **J.A. Hainfellner:** None. **M. Hartenbach:** None. **A.S. Berghoff:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Daiichi Sankyo. B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; Roche. F. Consultant/Advisory Board; Modest; Bristol-Myers Squibb, Daiichi Sankyo, Merck, Roche. Other; Modest; Amgen, Roche, AbbVie. **N.L. Albert:** B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; Novocure. F. Consultant/Advisory Board; Modest; Novartis, Advanced Accelerator Applications, Servier, Telix Pharmaceuticals. **M. Preusser:** F. Consultant/Advisory Board; Modest; Bayer, Bristol-Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMC Contrast, GlaxoSmithKline, Mundipharma, Roche, BMJ Journals, MedMedia, AstraZeneca, AbbVie, Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dohme, Tocagen, Adastra, Gan & Lee Pharmaceuticals, Janssen, Servier, Miltenyi, Boehringer-Ingelheim, Telix, Medscape.

Abstract Number: 40
Abstract Title: ***Translating immunoPET imaging of PD-L1 in glioblastoma: journey from the laboratory to clinical practice***

Authors:
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Background:
Inhibiting immune checkpoints (ICPs) has shown promise in reactivating the body's natural anti-cancer immune defences against different types of cancer. Yet, establishing an effective treatment protocol with these drugs for glioblastoma (GBM) has proven challenging. GBM has elevated expression of programmed death-ligand 1 (PD-L1), which correlates with its immunosuppressive and aggressive nature. Currently, there is no standardised method for assessing PD-L1 expression in brain tumours. To address this gap, we investigated immuno-PET using ^{89}Zr-radiolabelled Atezolizumab to quantify PD-L1 expression both in preclinical and clinical settings.
Material and Methods:
^{89}Zr-DFO-Atezolizumab was characterised *in vitro* and tested in mice bearing GBM tumours. PET/CT images were taken 24-72 h post-injection. Biodistribution, IHC, and flow cytometry were performed on tumour samples. ^{89}Zr-DFO-Atezolizumab (37 MBq) was administered to patients with newly diagnosed GBM (n=6; NCT05235737), with and w/o neoadjuvant pembrolizumab. PET/CT scans were performed 48-72 h post-injection. Radioconjugate uptake was measured in tumours and normal tissues. Tumour samples were collected post-surgery for analysis.
Results:
^{89}Zr-DFO-Atezolizumab was produced in high radiochemical purity and yield. *In vitro* cell-associated radioactivity correlated to the levels of PD-L1 expression in GBM cells, confirming the specificity of the radioconjugate. ^{89}Zr-DFO-Atezolizumab provided *in vivo* high contrast images of PD-L1 positive GBM brain tumours at 24 h and 48 h post-injection. Immunophenotyping of tumours revealed enrichment of PD1^{+} Tregs and PD-L1^{+} myeloid populations. In control patients, we observed high and heterogeneous accumulation of ^{89}Zr-DFO-Atezolizumab 48 h post-injection. Interestingly, in patients who received neoadjuvant pembrolizumab treatment, tumour uptake was less prominent. High uptake in normal tissues was found in the spleen, kidneys, and liver.^{89}Zr-DFO-Atezolizumab tumour targeting was positively correlated with tumour PD-L1 IHCs staining.
Conclusion:
Highly specific detection of tumour PD-L1 expression levels in GBM is achievable using ^{89}Zr-DFO-Atezolizumab. Immuno-PET imaging offers additional insights complementing *ex vivo* tumour and immune cell PD-L1 analysis.

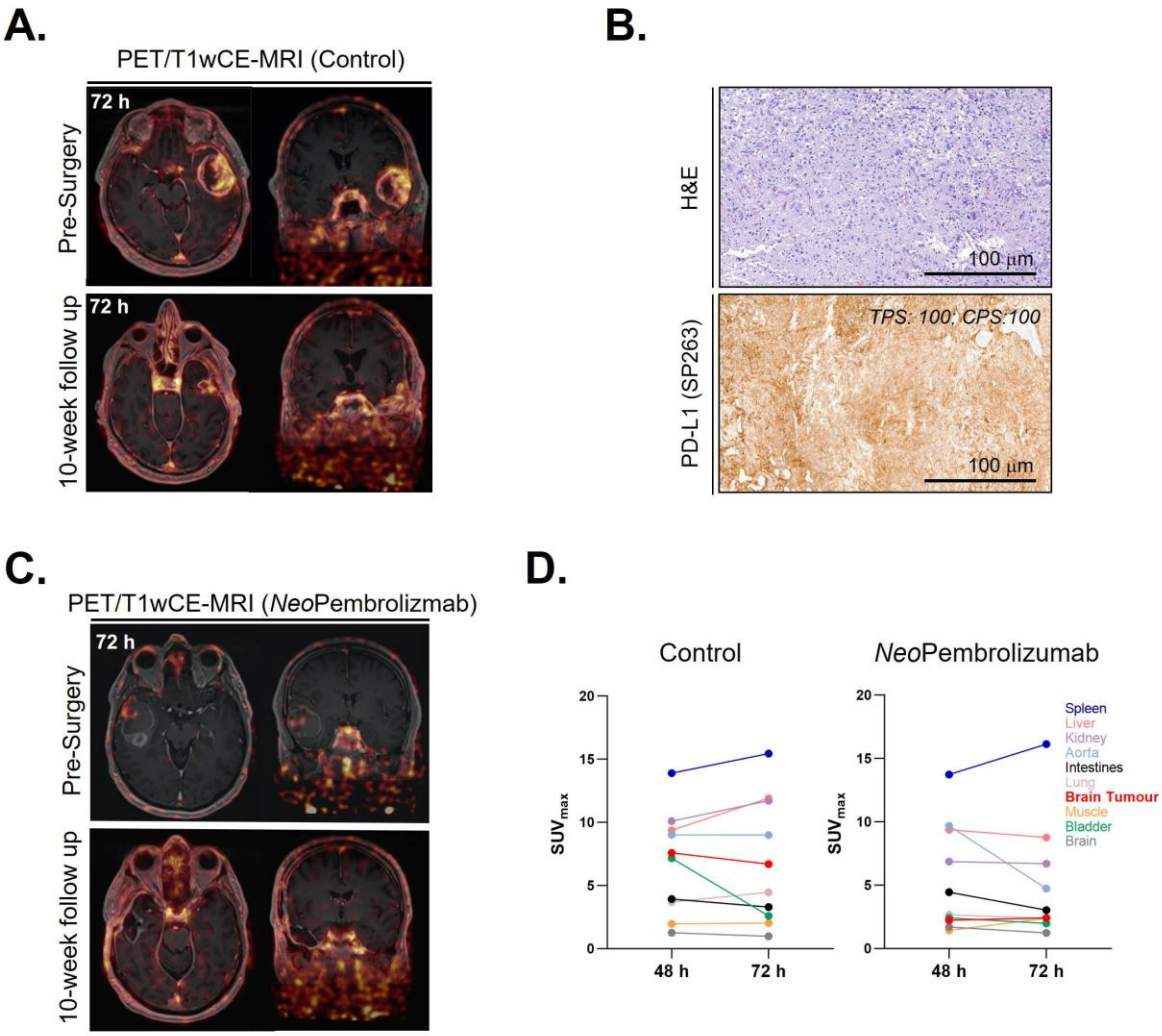

Figure 1: (A) Representative axial and coronal PET/MRI images of ^{89}Zr-DFO-Atezolizumab control patient uptake at 72 h post-injection prior to surgery and 10 weeks after surgery **(B)** Representative images of H&E and PD-L1 IHC stained biopsy tissue taken from control patient prior to surgery. **(C)** Representative axial and coronal PET/MRI images of ^{89}Zr-DFO-Atezolizumab neoadjuvant patient uptake at 72 h post-injection prior to surgery and 10 weeks after surgery **(D)** Representative tissue biodistribution of ^{89}Zr-DFO-Atezolizumab (SUV_{max}) from control and neoadjuvant pembrolizumab-treated patient taken 48 h and 72 h post-injection.

Author Disclosures:
D. Dar: None. **A. Kastelik-Hryniewiecka:** None. **C. Da Pieve:** None. **I. Gorczewska:** None. **G. Sharma:** None. **M. Niedbala:** None. **P. Bzowski:** None. **E. Chmielik:** None. **A. d'Amico:** None. **B. Bobek-Bilewicz:** None. **R. Tarnawski:** None. **E. Nowicka:** None. **W. Kaspera:** None. **G. Kramer-Marek:** None.

Abstract Number: 41
Abstract Title: *PET probe development for the Sigma2 receptor imaging in brain tumours - Preclinical evaluation of [^{18}F]RM273*

Authors:
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Background:
The sigma2 receptor (TMEM97) expression correlates well with the Ki67 expression in tumours [1, 2] and is therefore an attractive marker of the proliferative status. We developed the ^{18}F-labelled radioligand [^{18}F]RM273 for sigma2 receptor imaging in brain tumours.
Material and Methods:
[^{18}F]RM273 (2-[4-(6-[18F]fluoro-1H-pyrrolo[2,3-b]pyridin-1-yl)butyl]-6,7-dimethoxy-1,2,3,4-tetra-hydroisoquinoline) has been obtained by automated synthesis by Cu-mediated oxidative radiofluorination of the aryl boronic acid pinacol ester precursor. Radiometabolite analysis was performed in mouse plasma samples 30 min p.i. The target specificity was investigated by *in vitro* autoradiographic studies using the sigma2 receptor antagonist ISO-1 in rat brain cryosections with a stereotactically implanted F98 glioma [3]. The biodistribution of [^{18}F]RM273 in healthy mice (female, CD1; n = 4; 7.2 ± 1.1 MBq) and its tumour uptake into the F98 glioma (male, Fischer rats; n = 2; 21 and 25 MBq) were investigated by dynamic PET imaging for 60 min (nanoScan®PET-1T MRI, Mediso).
Results:
Polar radiometabolites of [^{18}F]RM273 (RCY: 8%, A_M: 69 - 233 GBq/µmol) were detectable in plasma, but not in brain extracts. We determined a 3-fold higher density of binding sites in tumour compared to healthy brain [3]. PET studies revealed a TAC peak value of 1.3 at 2.25 min p.i. followed by a wash out in the brain of healthy mice [3]. In the F98 glioma brain region a two-fold increase in uptake (SUV_{mean} of 0.8 - 1.3 at 30 - 60 min p.i.) was observed compared to the contralateral region.
Conclusion:
The results indicate that [^{18}F]RM273 could potentially be used for determining the proliferative status of brain tumours.
Acknowledgements:
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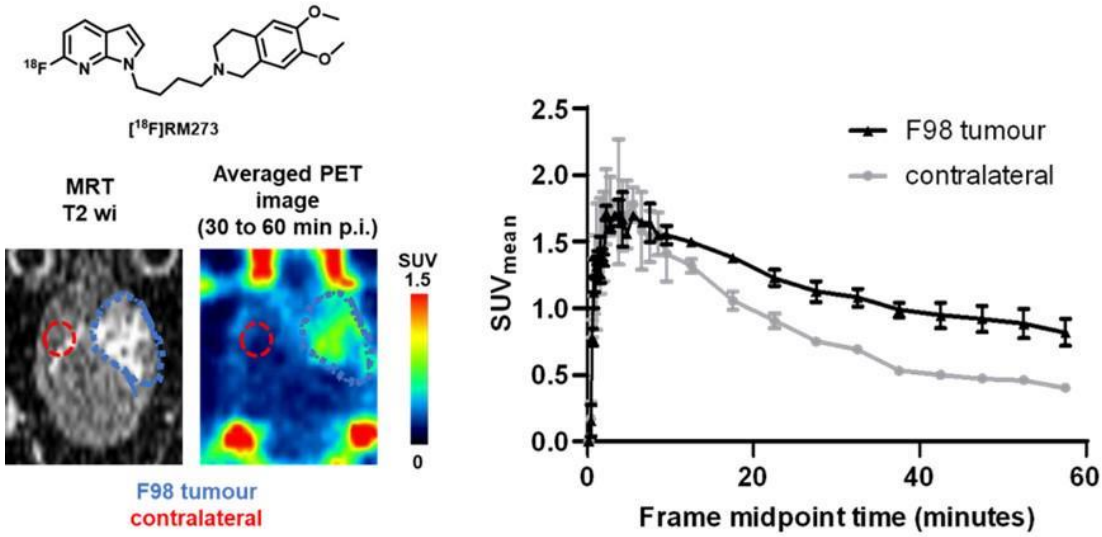
References:
[1] Shoghi et al. Plos One 2013, 8: e74188; [2] Yang et al. Molecules 2020, 25 (22): 5439 [3] Moldovan et al. Int. J. Mol. Sci. 2021, 22: 5447



[^{18}F]RM273 PET imaging of F98 glioma in rat. [^{18}F]RM273 has been intravenously injected into male F344 rats with intracranially implanted F98 glioma.

Author Disclosures:
D. Guendel: None. **M. Toussaint:** None. **R. Moldovan:** None. **R. Teodoro:** A. Employment (full or part-time); Significant; Life Molecular Imaging GmbH. **D. Schepmann:** None. **B. Wünsch:** None. **F. Ludwig:** None. **S. Fischer:** None. **P. Brust:** None. **W. Deuther-Conrad:** None.

Abstract Number: 42
Abstract Title: ***Impact of FET-PET imaging in surveillance of theranostic treatment with 4-L-[131I]iodo-phenylalanine ([131I]IPA) in relapsed glioblastoma patients***

Authors:
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Background:
Imaging glioblastoma (GBM) plays a critical role in disease evaluation and follow up. Contrast-enhanced magnetic resonance imaging (CE-MRI) is the modality of choice for characterizing GBM; however, CE-MRI often fails to distinguish clear tumor delineation from treatment-related changes, discrimination of pseudoprogression from real progression or pseudoresponse in patients on antiangiogenic therapy. O-(2-[^{18}F]fluoroethyl-)-L-tyrosine (^{18}F-FET) positron emission tomography (PET) has become a valuable tool for brain tumor surveillance,adding additional metabolic information in above mentioned uncertain MRI investigations.
Material and Methods:
We evaluated 12 patients treated in our center within study protocols IPAX 1 and IPAX Linz (clinicaltrials.gov ID NCT03849105 (IPAX-1) and EudraCT Number: 2021-006426-43 (IPAX-L) to compare advanced MRI imaging techniques with FET-PET in follow up investigations after treatment with theranostic therapy using 4-*L*-[131I]iodo-phenylalanine ([^{131}I]IPA) with additional external radiotherapy in relapsed Glioblastoma. This treatment was first investigated worldwide in glioblastoma. Molecularly targeted radiation (MTR) is a novel therapeutic approach that utilizes a specific molecular target to deliver a radionuclide payload to tumor cells. MRI imaging followed a standardized tumor protocol. FET PET static image acquisition parameters followed the recommendations of practice guidelines for imaging of gliomas using PET with radiolabeled amino acids. Additional SPECT imaging following infusion of 131I-IPA was performed post injection to determine the concentration of 131I-IPA in the tumor and normal brain. For this purpose, we use standardized PET analysis criteria as published in the literature to evaluate the validity and predictive value of additional FET-PET imaging in treatment surveillance after this new theranostic treatment approach. Assessment of treatment with MRI followed the mRANO criteria. Comparison of MRI and FET-PET imaging for discrimination of progression versus treatment related changes was done because there is lack of knowledge using two radiation treatment modalities in relapsed glioblastoma.
Results:
Presented at the meeting.
Conclusion:

Presented at the meeting.

Author Disclosures:
J. Pichler: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; TELIX Pharmaceuticals. F. Consultant/Advisory Board; Modest; TELIX Pharmaceuticals. **T. Traub-Weidinger:** None. **J. Feichtinger:** None. **J. Dierneder:** None. **R. Pichler:** None. **H. Geinitz:** None. **I. Höllmüller:** None. **R. KLeiser:** None. **S. Wimmer:** None. **M. Sonnberger:** None. **O. Osipova:** None. **A. Leibetseder:** None.

Abstract Number: 43
Abstract Title: ***Radiomic analysis of conventional MRI for the prediction of F-DOPA PET uptake characteristics in patients with brain metastases following stereotactic radiosurgery***

Authors:
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Background:
Amino acid PET has higher accuracy than conventional MRI in classifying post-treatment changes of brain metastases following stereotactic radiosurgery (SRS). We tested whether radiomic analysis of MRI data can predict the F-DOPA uptake parameters tumor-to-background ratio (TBR) and relative standardized uptake value (rSUV).
Materials and Methods:
We analyzed 82 patients with a total of 93 brain metastases from various primaries undergoing F-DOPA PET/CT for suspected radiological progression following SRS. Corresponding MRI acquisitions (± 4 weeks) included gadolinium-enhanced T1-weighted (ce-T1w) and T2-weighted FLAIR sequences. Radiomic features were extracted from the tumor zone, either from the original MRI image or after applying Wavelet filter using PyRadiomics (v3.0.1). MRI-derived features were then used to predict F-DOPA TBR and rSUV, binarized according to the thresholds 1.6 and 2.0. Prior to model training, select k best algorithm was applied for feature selection. Several Machine Learning (ML) models were used for the analysis using a hyperparameter optimization technique. Ten repetitions of a Stratified-K-Fold cross validation were used to extract results. Classification accuracy of the best-performing model was assessed by ROC curve analysis.
Results:
ce-T1w features achieved a ROC area under the curve (AUC)=0.86 for the prediction of TBR 1.6 threshold, with no improvement following the integration of FLAIR. For the prediction of rSUV 1.6 threshold, features extracted from ce-T1w achieved an AUC=0.7, which increased up to AUC = 0.85 with the additional information from FLAIR. AUC = 0.79 and AUC = 0.72 were obtained using ce-T1w features for prediction of TBR 2.0 and rSUV 2.0 thresholds, respectively, without substantial improvements from the addition of FLAIR. Support Vector Machine (SVM) with a linear kernel was the best-performing ML model.
Conclusion:
In our cohort, radiomic features extracted from conventional MRI could classify F-DOPA uptake with fair/good accuracy, with differences depending on the parameter and the threshold used.

Author Disclosures:

M. Cannistrà: None. **P. Vizza:** None. **G. Tradigo:** None. **L. Carideo:** None. **A. Bozzao:** None. **A. Romano:** None. **G.L. Cascini:** None. **G. Minniti:** None. **P. Veltri:** None. **F. Cicone:** None.

Abstract Number: 44
Abstract Title: *Differential gradients in neoplastic and inflammatory cell populations within peritumoural regions in high grade glioma a dual PET tracer and MRI study*

Authors:
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Objective:
Peritumoral microstructural changes in high-grade glioma were assessed with MRI and PET using diffusion tensor imaging (DTI) and the radiotracers [^{11}C](*R*)PK11195 for translocator protein (TSPO) and [^{11}C]methionine for amino acid transport and metabolism.
Material and Methods:
Dynamic PET and DTI data were acquired for twelve participants with primary high-grade glioma. Two masks were defined: tumour bulk representing the necrotic core and contrast enhancement (CE); and a peritumoural region defined as 5 mm from the CE edge. [^{11}C](*R*)PK11195 binding potential (BP) maps were calculated representing TSPO specific binding. [^{11}C]methionine uptake was expressed as tumour-to-background ratio (TBR). Probabilistic tractography analysis was performed using FSL tools with the peritumoural mask serving as the seed region (**Figure 1**). This allowed derivation of the average track length or average connectivity distance up to the seed mask in millimeters. TSPO binding and [^{11}C]methionine uptake along the tracks were then assessed by plotting each PET measure against the connectivity distance (**Figure 2**).
Results:
This preliminary analysis of data from three participants showed that along diffusion tracks [^{11}C](*R*)PK11195 binding and [^{11}C]methionine uptake were highest within the first 15 mm from the tumour edge. [^{11}C](*R*)PK11195 binding then steadily declined (**Figure 2. A**) and remained high (BP above 0.17 threshold) in two of the three participants beyond 30 mm distance. [^{11}C]methionine TBR remained above the 1.7 threshold up to 30 mm from the tumour edge and then rapidly decreased below the tumour threshold (**Figure 2. B)**.
Conclusion:
Using a novel combined DTI tractography and PET analysis, differences in neoplastic and inflammatory tissue extent in peritumoural regions around high-grade glioma were found.

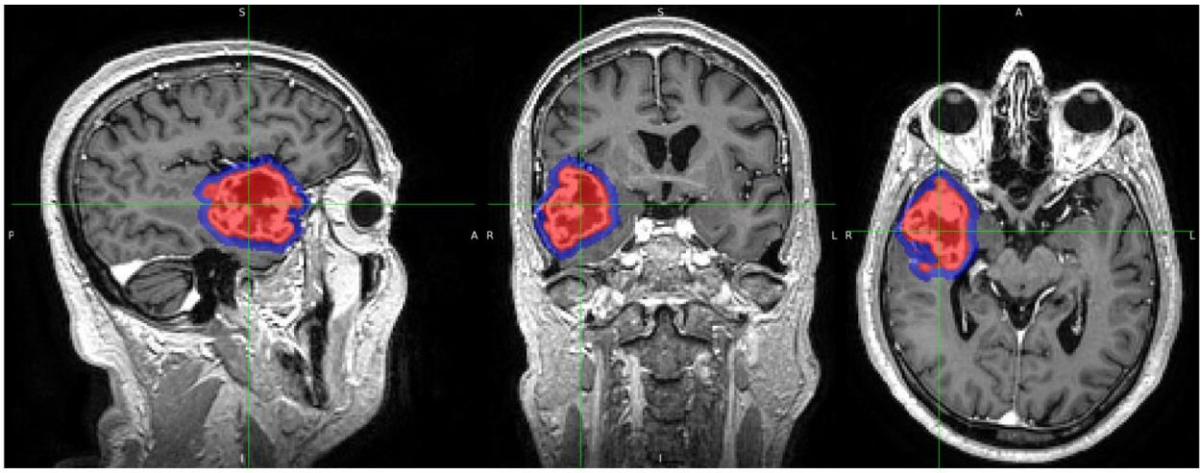

Figure 1 : example with wild-type glioblastoma showing the tumour bulk (red) and peritumoral (blue) masks overlaid on post-gadolinium T1 weighted MRI.

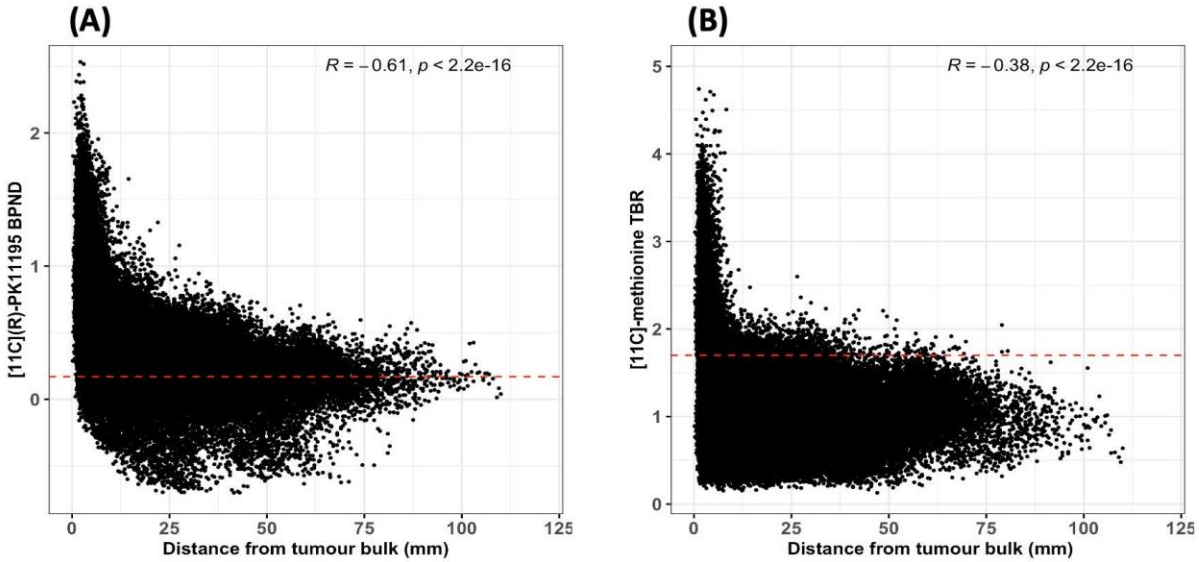

Figure 2 : Scatterplots showing each PET measure against the distance. **(A)** [^{11}C](*R*)PK11195 binding potential (BP_{ND}) and **(B)** [^{11}C]methionine tumour-to-background ratio (TBR) distributions along the diffusion connectivity distance (mm) from the tumour bulk. The red dashed line shows the threshold values (BP>0.17) for specific TSPO binding and (TBR>1.7) for [11C]methionine uptake.

Author Disclosures:
B.Q. Alfaifi: None. **E. Agushi:** None. **A. Jackson:** None. **D. Lewis:** None. **R. Hinz:** None. **D. Coope:** None.

Abstract Number: 45
Abstract Title: ***Assessment of response to lomustine-temozolomide chemotherapy in addition to radiotherapy in patients with newly diagnosed glioblastoma using FET PET***

Authors:
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Background:
We examined the value of *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (FET) PET for early response assessment in patients with newly diagnosed glioblastoma and methylated O^6-methylguanine-DNA methyltransferase promoter treated with lomustine-temozolomide chemotherapy in addition to radiotherapy.
Material and Methods:
Thirty-one patients (age range, 29-74 years) were treated according to the CeTeG/NOA-09 phase-3 trial. FET PET and anatomical MRI were performed at baseline and follow-up after the third cycle. We obtained mean and maximum tumor-to-brain ratios (TBR). Thresholds derived from FET PET were defined using ROC analyses to predict progression-free survival (PFS) of ≥12 months. The predictive value of FET PET parameters was subsequently assessed using univariate and multivariate survival estimates. MRI response assessment was based on RANO 1.0 criteria. The FET PET data were also used to evaluate response according to the recently proposed PET RANO 1.0 criteria.
Results:
As of January 2024, tumor progression was confirmed in 24 patients (77%). Patients received a median number of 6 cycles of lomustine-temozolomide chemotherapy (range, 3-6 cycles). After treatment initiation, the median follow-up was 15.0 months (range, 7.2-59.4 months). After three cycles of lomustine-temozolomide, a reduction of maximum TBR values by ≥10% predicted a significantly longer PFS (29.9 vs. 9.9 months; P=0.042). In contrast, changes in mean TBR values, RANO 1.0 criteria, and PET RANO 1.0 criteria were not predictive for response (P>0.05). Multivariate survival analysis revealed that changes in maximum TBR predicted a significantly prolonged PFS independent of age, the extent of resection, and the Karnofsky Performance Status (P=0.039; HR, 2.697; 95% CI, 1.074-7.298).
Conclusion:
Unlike RANO 1.0 criteria and PET RANO 1.0 criteria, our results suggest that FET PET parameters are clinically valuable for identifying responders to lomustine-temozolomide chemotherapy in addition to radiotherapy early after treatment initiation. The evaluation to predict a significantly longer overall survival is ongoing.

Author Disclosures:
J. Werner: None. **M.M. Wollring:** None. **C. Tscherpel:** None. **E.K. Rosen:** None. **G. Ceccon:** None. **I. Stetter:** None. **P. Lohmann:** None. **J. Weller:** None. **G. Stoffels:** None. **C. Baues:** None. **E. Celik:** None. **F.M. Mottaghy:** None. **R. Goldbrunner:** None. **U. Herrlinger:** None. **G.R. Fink:** None. **K. Langen:** None. **N. Galldiks:** None.

Abstract Number: 49
Abstract Title: ***FET PET uptake characteristics in* IDH-*mutant glioma***

Authors:
E. Barci[1], R. Forbrig[2], K. Müller[3], S. Kunte[1], L. Kaiser[1], C. Schichor[4], P. Harter[5], M. Preusser[6], L. von Baumgarten[4], N. Thon[4], N. L. Albert[1];
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Background:
Contrast enhancement in MRI correlates to response to treatment with the IDH inhibitor vorasidenib in *IDH*-mutant glioma. Tracer uptake on amino acid PET with FET is associated with tumor type and malignancy in gliomas. We investigated the correlation of contrast media and FET uptake in newly diagnosed *IDH*-mutant glioma as a basis for future biomarker studies for refined prediction of vorasidenib efficacy.
Material and Methods:
Patients with histologically verified *IDH*-mutant glioma WHO grade 2-4 (WHO 2021 classification) without prior radio- and / or chemotherapy were included. Static FET PET parameters (maximal and mean tumor-to-background ratios (TBR_{max} and TBR_{mean}) and PET volume were evaluated and compared to contrast-enhanced MRI as well as neuropathological diagnosis. PET and MRI-based volumes (contrast-enhancing volume; T2 volume) were compared visually.
Results:
Overall, 44/148 (29.7%) cases showed contrast enhancement on MRI. On FET PET, 98/148 (66.2%) cases were FET-positive with a higher proportion in oligodendrogliomas (63/69 (91.3%)) compared to astrocytomas (35/79 (44.3%)). Both, presence of contrast enhancement as well as FET uptake showed a positive correlation with the WHO grade, however, with a high overlap of TBR_{max} and TBR_{mean} values between WHO grades. Among the gliomas without contrast enhancement on MRI, 58/104 (55.8%) presented with FET uptake, and vice versa, 4/44 (9.1%) of the contrast-enhancing gliomas were FET-negative. Areas of FET uptake significantly exceeded areas of contrast enhancement in 25/44 (56.8%) cases.
Conclusion:
FET PET provides complementary information to contrast-enhanced MRI in *IDH*-mutant glioma and therefore should be explored as additional biomarker. Future studies should put PET positivity into relation to response to IDH inhibitor therapy.

Author Disclosures:
E. Barci: None. **R. Forbrig:** None. **K. Müller:** None. **S. Kunte:** None. **L. Kaiser:** None. **C. Schichor:** None. **P. Harter:** None. **M. Preusser:** F. Consultant/Advisory Board; Modest; Bayer, Bristol-Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMC Contrast, GlaxoSmithKline, Mundipharma, Roche, BMJ Journals, MedMedia, Astra Zeneca, AbbVie, Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dome, Tocagen, Adastra, Gan & Lee Pharmaceuticals, Janssen, Servier, Miltenyi, Böhringer-Ingelheim, Telix, Medscape. **L. von Baumgarten:** None. **N. Thon:** None. **N.L. Albert:** B. Research Grant (principal investigator, collaborator

or consultant and pending grants as well as grants already received); Significant; Novocure. F. Consultant/Advisory Board; Modest; Novartis, Advanced Accelerator Applications, Servier and Telix Pharmaceuticals.

Abstract Number: 50
Abstract Title: ***Survival prediction for glioma patients at initial diagnosis using multimodal radiomics***

Authors:
L. Kaiser[1], S. Quach[2], A. J. Zounek[1], A. Zatcepin[1], A. Holzgreve[1], S. Kirchleitner[2], V. C. Ruf[3], M. Brendel[1], N. Thon[2], J. Herms[3], M. Riemenschneider[4], S. Stöcklein[5], M. Niyazi[6], R. Rupprecht[7], J. Tonn[2], P. Bartenstein[1], S. Ziegler[1], L. von Baumgarten[2], N. L. Albert[1];
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Background:
Individuals with glioblastoma encounter poor survival outcomes despite comprehensive treatments. The use of PET imaging for glioma characterization and treatment planning is on the rise. This study assesses the predictive significance of multimodal radiomics analyses in glioblastoma patients at initial diagnosis and contrasts various techniques (FET-PET, TSPO-PET, and MRI).
Material and Methods:
This study included 40 glioblastoma patients who underwent multimodal imaging before radiation therapy. Analyzed images included: 5-15 and 20-40 min p.i. FET-PET, 60-80 min p.i. TSPO-PET, contrast-enhanced (CE) T1-MRI, and T2-MRI. PET and MRI static images were normalized to healthy background signal (TBR). Additionally, time-to-peak and slope images were derived from dynamic FET-PET. MRI volumes were defined using the BraTS Toolkit, while PET volumes were delineated using a TBR isocountour (1.6). Cox's proportional hazards model with elastic net fine-tuning was used for predicting overall survival, and C-indices (CI) were derived using 5-fold, 5-repeated cross-validation (CV). L1 ratio and Alpha were optimized within a nested CV scheme.
Results:
In univariate analysis, texture parameters (max. 0.78; 14% with CI>0.7) and shape parameters (0.74; 71%) from TSPO images yielded the highest C-indices. Evaluating individual modalities in multivariate analysis, the TSPO model showed a higher CI (0.75±0.17) compared to other techniques (FET20-40 0.67±0.15; CE T1 0.64±0.12; T2 0.55±0.13). In multimodal multivariate analysis, a combination of parameters from all modalities received highest coefficients but did not exceed the performance of TSPO-PET alone.
Conclusion:
TSPO-PET radiomics emerged as the most predictive in terms of prognosis when compared to other modalities. The integration of various modalities did not enhance the prognostic value in this group of patients. These results need to be validated in larger and more diverse cohorts, especially with respect to the prognostic value of a combination of different modalities.

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L. Kaiser: None. **S. Quach:** None. **A.J. Zounek:** None. **A. Zatcepin:** None. **A. Holzgreve:** None. **S. Kirchleitner:** None. **V.C. Ruf:** None. **M. Brendel:** None. **N. Thon:** None. **J. Herms:** None. **M.**

Riemenschneider: None. **S. Stöcklein:** None. **M. Niyazi:** None. **R. Rupprecht:** None. **J. Tonn:** None. **P. Bartenstein:** None. **S. Ziegler:** None. **L. von Baumgarten:** None. **N.L. Albert:** None.

Abstract Number: 51
Abstract Title: ***Analysis of tumor relapse probability and overall survival prediction following concomitant radiotherapy with temozolomide using FET PET in patients with glioblastoma***

Authors:
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Background:
Early after surgery and completion of concomitant radiotherapy with temozolomide, the evaluation of tumor relapse probability and overall survival prediction is of considerable interest for the management of patients with glioblastoma.
Material and Methods:
Sixty-three adult glioblastoma patients (mean age 55.4 years, SD ± 14.6) who received dynamic PET imaging using the radiolabeled amino acid *O*-(2-[^{18}F]fluoroethyl)-L-tyrosine (FET) after surgery or biopsy and completion of concomitant radiotherapy with temozolomide, were retrospectively included in the study. Static FET PET parameters such as maximum and mean tumor-to-brain ratios (TBR_{max}/TBR_{mean}) and metabolic tumor volumes (MTV) and the dynamic FET PET parameter time-to-peak (TTP) were obtained. The prognostic value of FET PET parameters was evaluated concerning the progression-free and overall survival (PFS, OS). Using receiver-operating-characteristic (ROC) analyses, threshold values for FET PET parameters were acquired. Subsequently, univariate and multivariate survival estimates were performed to assess the prognostic value of these parameters to predict a significantly longer PFS (as a surrogate for tumor relapse probability) and OS.
Results:
ROC analysis revealed that the parameter TBR_{max} was the most powerful parameter to predict both a significantly longer PFS (17.8 vs. 9.0 months; P=0.003; threshold, 2.85) and OS (33.2 vs. 18.4 months; P=0.002; threshold, 2.75). MTV had a similar prognostic value for both PFS (15.9 vs. 7.2 months; P=0.002; threshold, 34.0 mL) and OS (28.2 vs. 14.4 months; P=0.003; threshold, 32.6 mL). At a lower level of significance, TTP was only prognostic for a significantly longer OS (27.7 vs. 17.5 months; P=0.037; threshold, 25 minutes). TBR_{max} and MTV remained significant in multivariate survival analysis, indicating independent predictors for both a significantly longer PFS and OS (all P≤0.04).
Conclusion:
Our results suggest that FET PET parameters were highly prognostic in patients with newly diagnosed glioblastomas at an early stage of first-line therapy for predicting favourable PFS and OS.

Author Disclosures:
I. Stetter: None. **J. Werner:** None. **M. Wollring:** None. **G. Ceccon:** None. **P. Lohmann:** None. **G. Stoffels:** None. **F.M. Mottaghy:** None. **G.R. Fink:** None. **K. Langen:** None. **N. Galldiks:** None.

Abstract Number: 52

Abstract Title: ***CITADEL-123*. TRIAL IN PROGRESS *A Phase I clinical trial to assess the activity of I-123 Poly Adenosine Diphosphate Ribose Polymerase I inhibitor (123I-ATT001) directly administered in subjects with relapsed glioblastoma*.**

Authors:
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CITADEL-123: INTRODUCTION:

123I-ATT001, is a Targeted Radionuclide Therapy (TRT), consisting of a PARP 1-inhibitor (PARPi) that is radiolabelled with Iodine-123 (123I) to enable the targeted delivery of high-linear energy transfer (LET) Auger radiation (159 KeV/µm) to the tumour. Auger-emitting radionuclides have the potential to deliver extremely selective radiation within the nanometer range, which greatly reduces or eliminates the cross-fire effect, potentially reducing non-specific toxicities. Gliomas are the most common primary brain malignancies. The current standard of care includes surgical resection, supplemented by radiotherapy and chemotherapy, but the prognosis remains poor, with over 80% of patients recurring at the original resection site. PARP-1 has become a target of high interest for cancer treatment. PARPi bind to active PARP in close proximity to the DNA and block DNA damage repair pathways. Active PARP-1 is significantly increased in GBM, therefore, auger-emitting 123I-PARPi has the potential to become a therapeutic modality with a significantly reduced toxicity.

TRIAL DESIGN:

CITADEL-123 is a Phase I First-in-Human Therapy study of 123I-ATT001 as a monotherapy in patients with recurrent GBM. Eligible patients with recurrent GBM are eligible and must undergo Ommaya reservoir insertion in an intratumorally cavity with sufficient volume for drug infusion. 123I-ATT001 therapy begins 2-4 weeks post-operative procedure and is administered intratumorally weekly for 4 consecutive weeks. The study starts with a dose escalation with three planned dose levels according to a BOIN design, starting at 500MBq. The primary endpoint is the safety and tolerability of 123I-ATT001. Secondary endpoints include progression free survival by RANO criteria, survival and dosimetry. Up to 4 statistically powered expansion cohorts will explore 123I-ATT001 as monotherapy and in combination with other anti-tumour therapies for a longer treatment period. The study is opening in the UK this summer with European sites to follow.

Author Disclosures:

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Abstract Number: 53
Abstract Title: ***Application of the PET RANO 1.0 criteria in diffuse glioma: retrospective single center experience***

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Background:
Response evaluation in the treatment of glioma has been limited to MRI-based RANO criteria until the recent publication of the PET RANO 1.0 criteria. This study analyses longitudinal [18F]FET PET data of patients with diffuse glioma and applies the PET RANO 1.0 criteria to describe PET characteristics at baseline, response classes, and changes of individual parameters.
Methods:
In this retrospective single-center study, patients with diffuse glioma and a baseline as well as at least one follow-up [18F]FET PET scan were identified. PET analyses were performed according to the PET RANO 1.0 criteria and included the assessment of maximal and mean target-to-background ratios (TBRmax, TBRmean), PET volume, changes of these values between scans, and the presence of either measurable or no / non-measurable disease. Follow-up scans were classified as PET-based progressive disease (PET-PD), stable disease (PET-SD), partial response (PET-PR), or complete response (PET-CR) according to PET RANO 1.0.
Results:
A total of 532 scans in 154 patients were evaluated with a total of 235 treatment lines or follow-up evaluations without treatment. Overall, 171/235 baseline scans had measurable disease, 64/235 had non-measurable or no measurable disease. PET-PD was determined based on significant volume changes and/or occurrence of new lesions in the majority of cases (>90%), while significant increases of uptake intensity were found in 30% of cases. A sole increase of uptake intensity as determinant for PET-PD was found in 7% of PET-PD cases only. PET-PR was determined based on volume reductions in 84% of cases (23% in combination with decreasing uptake intensity), and by a sole reduction of uptake intensity in 16% of PET-PR cases.
Conclusion:
This study demonstrates that significant volume changes seem to be the major determinant for treatment response according to PET RANO 1.0 criteria and are often accompanied by changes of uptake intensity, while sole uptake intensity changes determine response classes only in a subset of patients. Further analyses will be performed taking into account the tumour entity, type of treatment and number of treatment line.

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