UNIVERSITÄTS KLINIKUM FREIBURG

CCCF COMPREHENSIVE CANCER CENTER FREIBURG

dkfz.

Deutsches Konsortium für Translationale Krebsforschung

Partnerstandort Freiburg

DKTK

PET-Bildgebung: Stellenwert und Empfehlungen für die Zielvolumendefinition in der kranialen Stereotaxie

Ilinca Popp und Anca-L. Grosu

Klinik für Strahlenheilkunde

Universitätsklinikum Freiburg

Inhalt

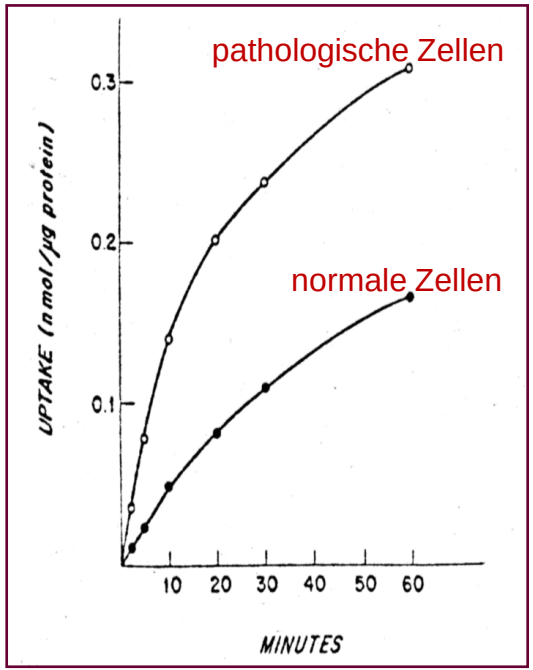
- Gliome
- Hirnmetastasen
- Meningeome
- Glomus Tumoren

Inhalt

- **Gliome**
- **Hirnmetastasen**
- **Meningeome**
- **Glomus Tumoren**

Gliome

Rationale für die Einbeziehung von AS-PET in die RT-Planung



Uptake α-aminoisobutyrat

- Hohes Uptake durch die L-/A- Aminosäure Transportsystem
- LAT überexprimiert in malignen Zellen (Gliome, Hirnmetastasen)

→ Gute Tumor/Background Ratio (TBR)

Isselbacher 1972

Gliome

Rationale für die Einbeziehung von AS-PET in die RT-Planung

Accuracy of amino acid PET for brain tumor delineation in comparison with histologic evaluation

Authors	N[1]	Technique	Sensitivity[2]	Specificity[2]
Braun	32	MET-PET	87% (26/30)	75% (3/4)
Pirotte	32	MET-PET	100% (61/61)	100% (9/9)
Kracht	30	MET-PET	87% (87/100)	89% (16/18)
Pauleit	31	FET-PET	93%[3]	94%[3]
		MRI[4]	96%	53%

[1]number of patients, [2]based on analyzed lesions or biopsies, [3] total of 52 samples, 26 positive for tumor tissue. Sensitivity and specificity were calculated from fitted receiver operator characteristic (ROC) curve. [4]Combined analysis of non-enhanced T1-weighted sequences, Gd-enhanced sequences and FLAIR sequences.(Weber 2008)

Differentiation of radiation necrosis and tumor recurrence by amino acid PET or SPECT

Authors	N	Technique	Sensitivity	Specificity
Rachinger	45	FET-PET	94% (29/31)	93% (13/14)
		MRI[1]	97%(30/31)	50% (7/14)
Tsuyuguch	21	MET-PET	78% (7/9)	100% (12/12)
Samnick	78	IMT-SPECT	94% (62/66)	100% (12/12)

[1]contrast enhancement in T1-weighted images after administration of Gadolinium-DTPA (Weber 2008)

Weber, Grosu et al. Nat CPO 2008

Gliome

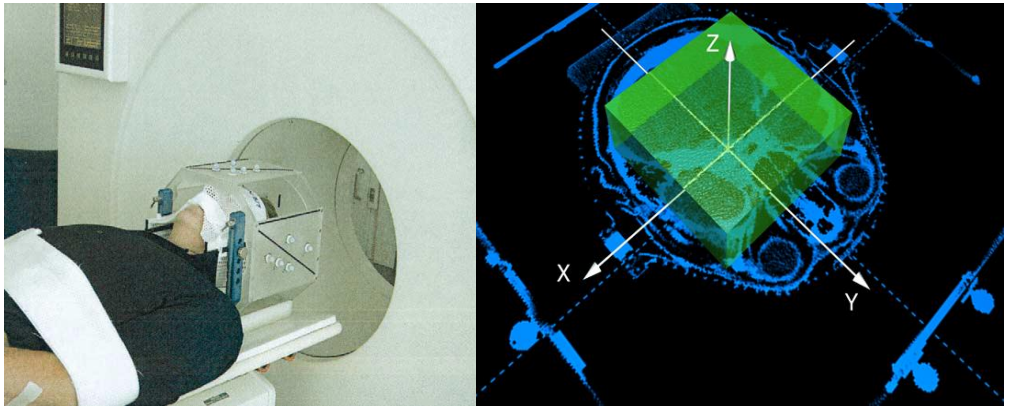
Qualität der Bildfusion zwischen PET und CT

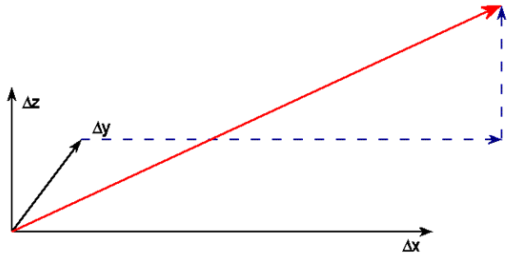
PHYSICS CONTRIBUTION

VALIDATION OF A METHOD FOR AUTOMATIC IMAGE FUSION (BRAINLAB SYSTEM) OF CT DATA AND ^{11}C-METHIONINE-PET DATA FOR STEREOTACTIC RADIOTHERAPY USING A LINAC: FIRST CLINICAL EXPERIENCE

Anca-Ligia Grosu, M.D.,* Rainer Lachner, Ph.D.,† Nicole Wiedenmann, M.D.,* Sibylle Stärk, Ph.D.,* Reinhard Thamm, M.D.,* Peter Kneschaurek, Ph.D.,* Markus Schwaiger, M.D.,‡ Michael Molls, M.D., Ph.D.,* and Wolfgang A. Weber, M.D.‡

Departments of *Radiation Oncology and ‡Nuclear Medicine, Technical University Munich, Munich, Germany; †BrainLAB GmbH Munich, Munich, Germany





Abweichung 2,3 mm
Rigide Fusion
Basierend auf *mutual information*

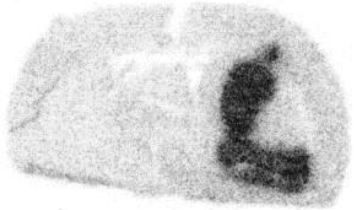
Grosu et al. IJROBP 2003

Gliome

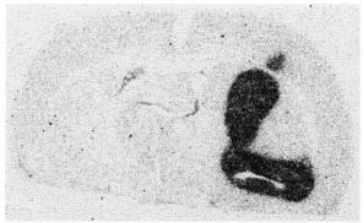
MET FDOPA FACBC

FET AMT IMT

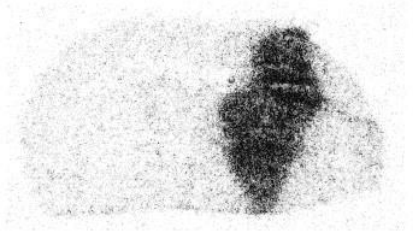
Wahl des Tracers



O-(2-[^{18}F]fluoroethyl)-L-tyrosine (FET)

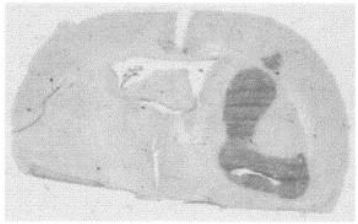


[^{3}H]-Methyl-L-methionine (MET)

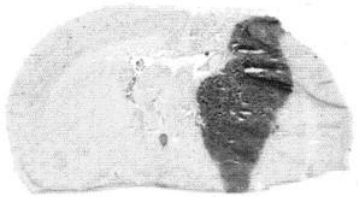


2-[^{18}F]fluoro-L-Tyrosine (FTyr)

[^{3}H]-Methyl-L-methionine (MET)



Cresyl-Violet-Staining



Cresyl-Violet-Staining

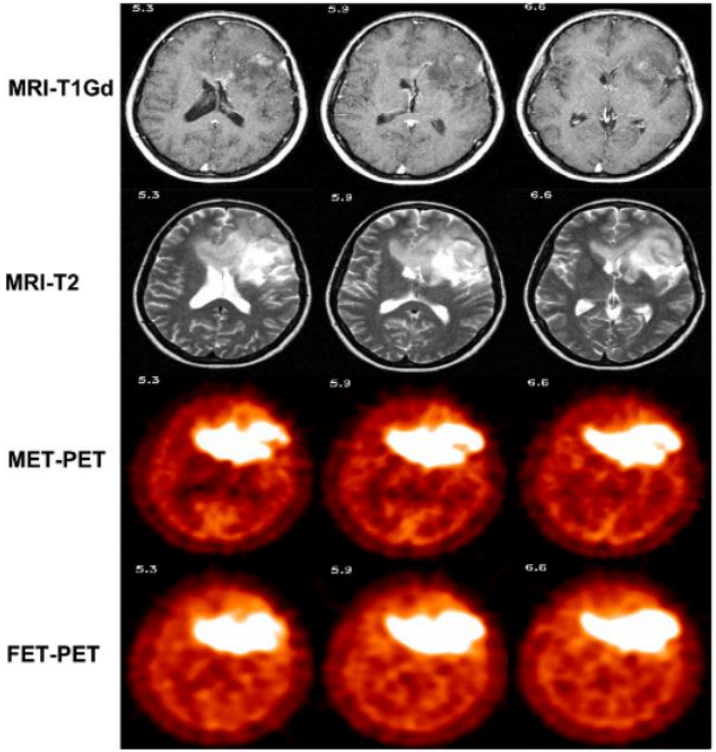
TBR bei MET, FET und FTyr in einem Gliom-Modell (Ratte)

UNIVERSITÄTS KLINIKUM FREIBURG

Langen et al., Nuc Med Biol, 2003

Gliome

Wahl des Tracers



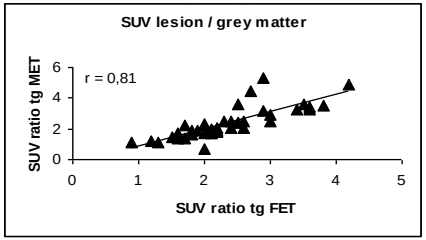
Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 4, pp. 1049–1058, 2011

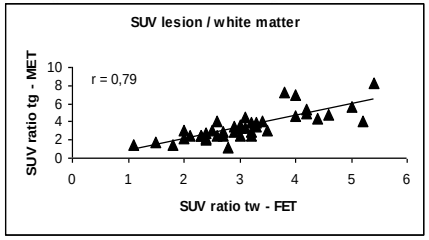
0360-3016/$ - see front matter

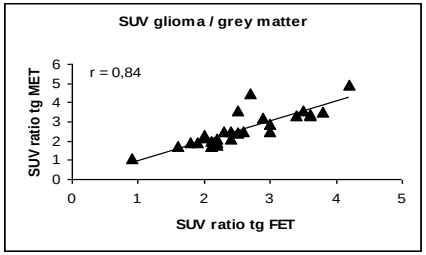
CLINICAL INVESTIGATION Brain

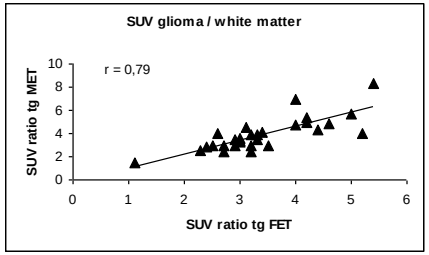
AN INTERINDIVIDUAL COMPARISON OF O-(2- [^{18}F]FLUOROETHYL)-L-TYROSINE (FET)– AND L-[METHYL-^{11}C]METHIONINE (MET)–PET IN PATIENTS WITH BRAIN GLIOMAS AND METASTASES

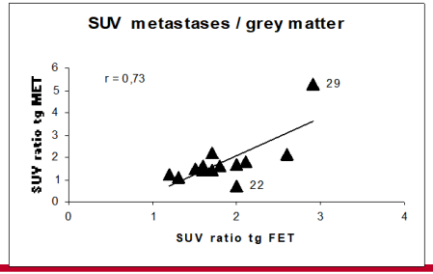
Anca-Ligia Grosu, M.D.,*† Sabrina T. Astner, M.D.,† Eva Riedel, M.D.,‡§ Carsten Nieder, M.D.,†‖ Nicole Wiedenmann, M.D.,*† Felix Heinemann, M.D.,* Markus Schwaiger, M.D.,‡ Michael Molls, M.D.,† Hans-Jürgen Wester, Ph.D.,‡ and Wolfgang A. Weber, M.D.‡¶

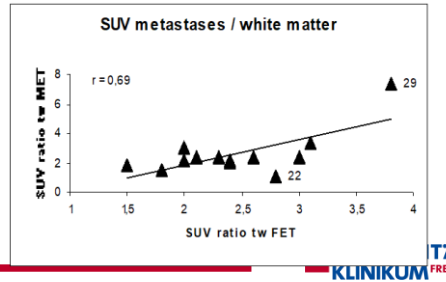






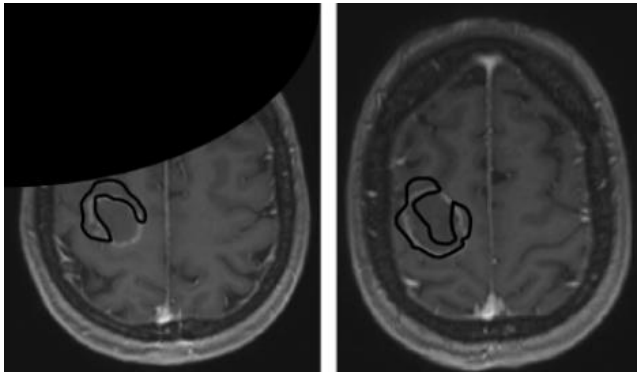






Gliome

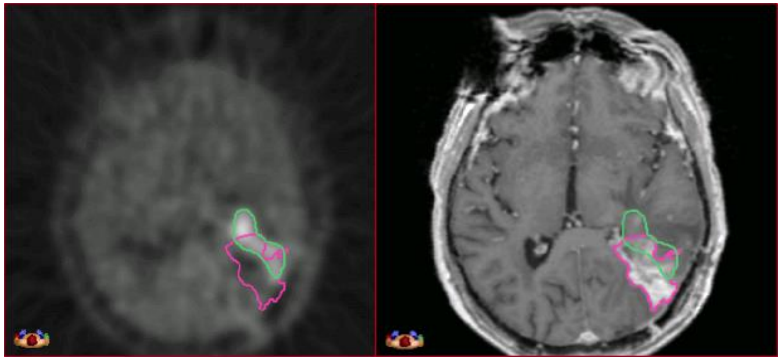
Zusätzliche Information durch AS-PET → BTV

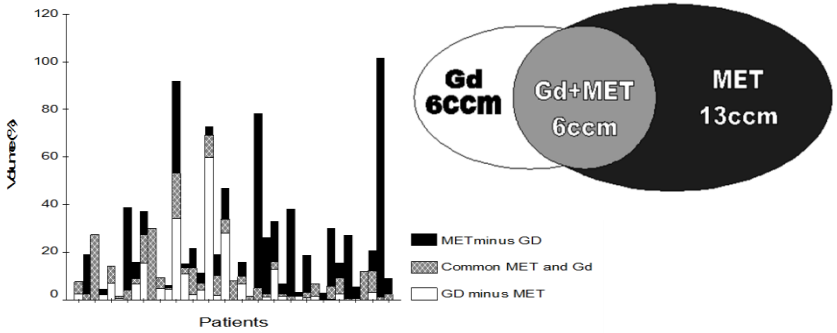


FET-PET TBR 1,5

Tumour volumes. Measurement of different tumour volumes in 17 glioblastoma patients.

BTV [cc]	BTV + 2 [cc]	GTV [cc]	CTV [cc]
Median 43.9	**Median 240.3**	**Median 34.1**	**Median 224.5**





Niyazi et al. Radiother Oncol 2011

Grosu et al. IJROBP 2005

Gliome

Zielvolumendefinition bei Re-Bestrahlung

Radiotherapy and Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

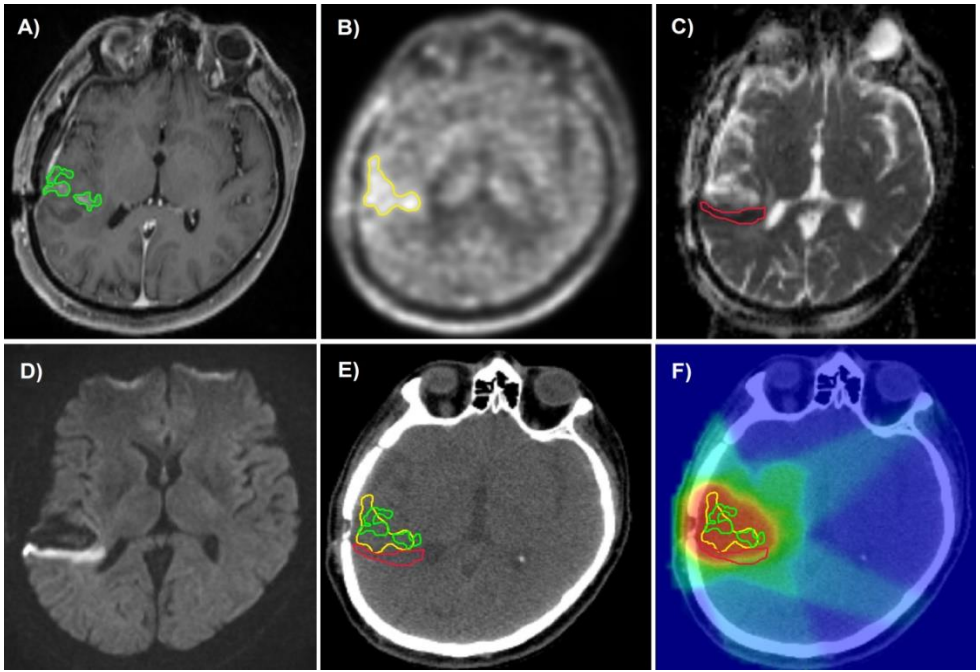
journal homepage: www.thegreenjournal.com

Original article

Diffusion-weighted MRI and ADC versus FET-PET and GdT1w-MRI for gross tumor volume (GTV) delineation in re-irradiation of recurrent glioblastoma

Ilinca Popp [a,*], Stefan Bott [a], Michael Mix [b,i], Oliver Oehlke [a,1], Tanja Schimek-Jasch [a], Carsten Nieder [c,d], Ursula Nestle [a,i,1], Michael Bock [e], William T.C. Yuh [f], Philipp Tobias Meyer [b,i], Wolfgang A. Weber [g,j], Horst Urbach [h], Irina Mader [h,2], Anca-Ligia Grosu [a,i,2]

[a] Department of Radiation Oncology; [b] Department of Nuclear Medicine, Medical Center – University of Freiburg, Germany; [c] Department of Oncology and Palliative Medicine, Nordland Hospital, Bodø; [d] Department of Clinical Medicine, Faculty of Health Sciences, University of Tromsø, Norway; [e] Department of Radiology, Medical Physics, Medical Center – University of Freiburg, Germany; [f] University of Washington School of Medicine, Department of Radiology, Seattle, USA; [g] Department of Nuclear Medicine, Klinikum rechts der Isar, Technical University of Munich; [h] Department of Neuroradiology, Medical Center – University of Freiburg; [i] German Cancer Consortium (DKTK), Partner Site Freiburg; and [j] German Cancer Consortium (DKTK), Partner Site Munich, Germany



41 Pat., SFRT 39 Gy à 3 Gy
AS-PET/CT/MRT Planung

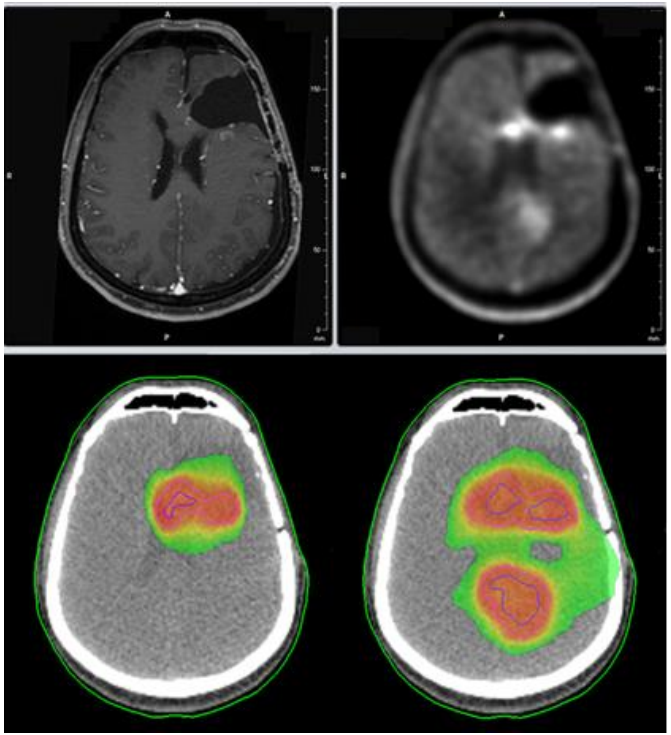
FET-PET → die beste Korrelation mit der Rezidiv-Lokalisation

UNIVERSITÄTS KLINIKUM FREIBURG

Popp et al. Radiother Oncol 2018

Gliome

GLIAA (NOA10) – prospektive, randomisierte, multizentrische Studie



Amino-acid FET-PET versus MRI guided re-irradiation in patients with recurrent GBM. A multicenter randomized phase II trial
(GLIAA) NOA10
PI: Prof. A.L.Grosu

Rezidiv GBM

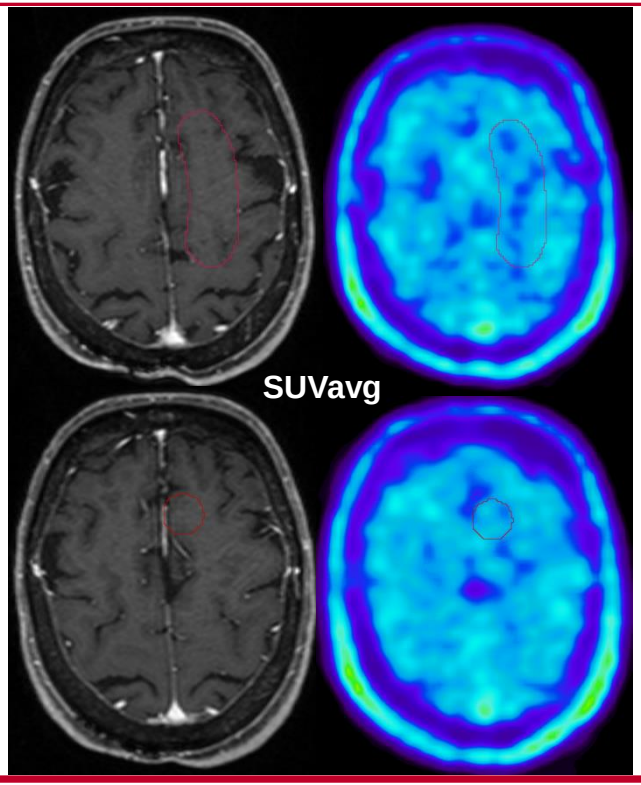
Arm A: Planung basierend auf FET-PET/CT
versus
Arm B: Planung basierend auf MRT

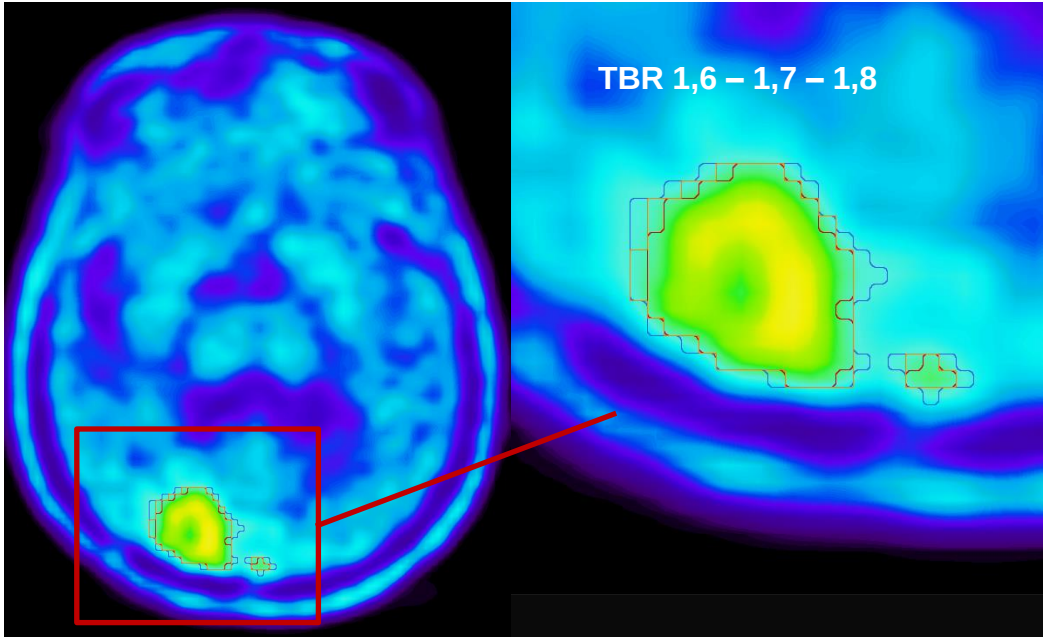
Primärer Endpunkt: PFS

200 Patienten
Studie abgeschlossen
Erste Ergebnisse Ende 2022

Gliome

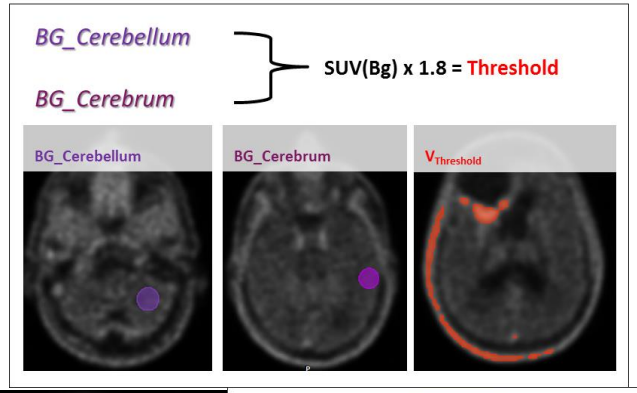
AS-PET für die Zielvolumendefinition bei ReRT

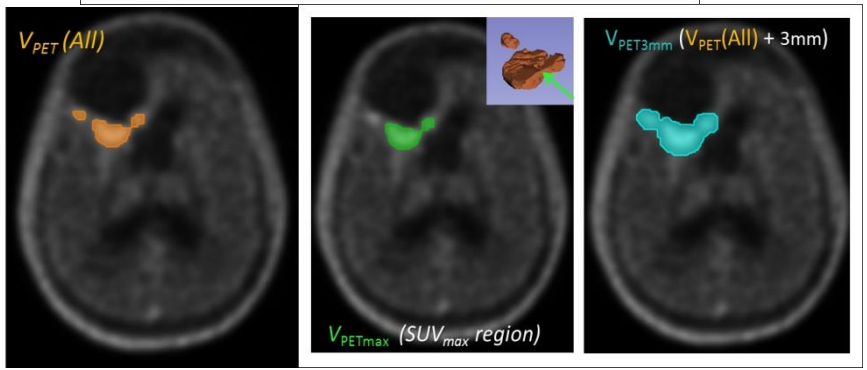


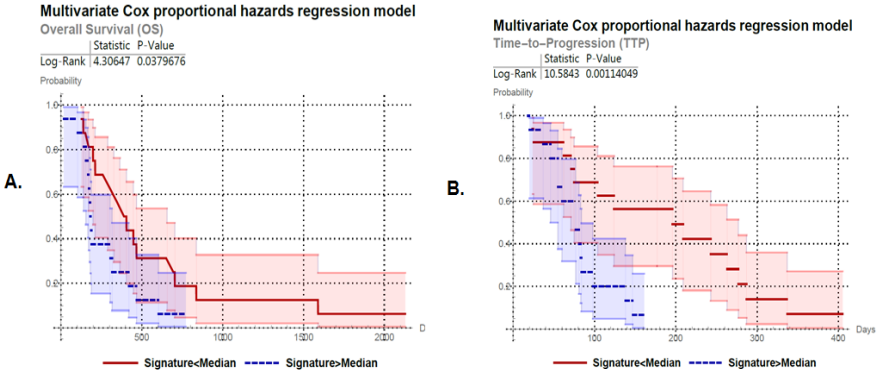


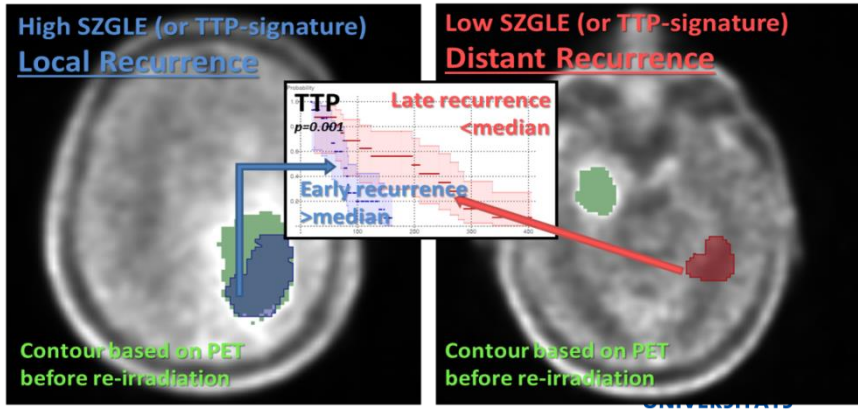
Gliome

Radiomics und künstliche Intelligenz









Carles, Popp, Grosu et al. Radiat Oncol 2021

Gliome

Empfehlungen

Neuro-Oncology
23(6), 881–893, 2021 | doi:10.1093/neuonc/noab013 | Advance Access date 4 February 2021

Contribution of PET imaging to radiotherapy planning and monitoring in glioma patients - a report of the PET/RANO group

Norbert Galldiks, Maximilian Niyazi, Anca L. Grosu, Martin Kocher, Karl-Josef Langen, Ian Law, Giuseppe Minniti, Michelle M. Kim, Christina Tsien, Frederic Dhermain, Riccardo Soffietti, Minesh P. Mehta, Michael Weller, and Jörg-Christian Tonn

	Amino Acid PET (MET, FET, FDOPA)	FDG PET	Other PET Tracers	Oxford Level of Evidence
Target delineation for radiotherapy planning	++	–	n.a.	2
Prognostic value of PET prior to radiotherapy	++	++	n.a.	2
PET-based radiotherapy in patients with newly diagnosed gliomas	(++)	n.a.	n.a.	3
PET-based re-irradiation in patients with glioma relapse	(++)	n.a.	n.a.	3
Assessment of response to radiotherapy	++	+	(++)	2
Differentiation of radiation injury from glioma relapse	++[a]	+	n.a.	2
Use of artificial intelligence for radiotherapy	(++)	n.a.	n.a.	3

Abbreviations: FDG, [^{18}F]-2-fluoro-2-deoxy-D-glucose; FDOPA, 3,4-dihydroxy-6-[^{18}F]-fluoro-L-phenylalanine; FET, *O*-(2-[^{18}F]-fluoroethyl)-L-tyrosine; MET, [^{11}C-methyl]-L-methionine.
++ high diagnostic value; (++) high diagnostic value, but limited data available; + limited diagnostic accuracy; – not helpful; n.a. = only preliminary or no data available.
[a]Increased accuracy when using dynamic FET PET.

Galldiks et al. Neuro-Oncol 2021

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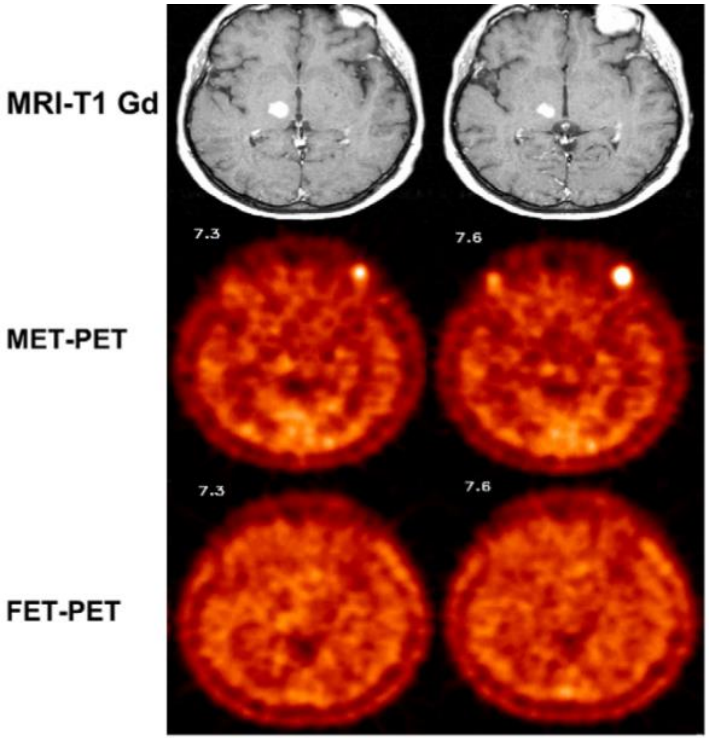
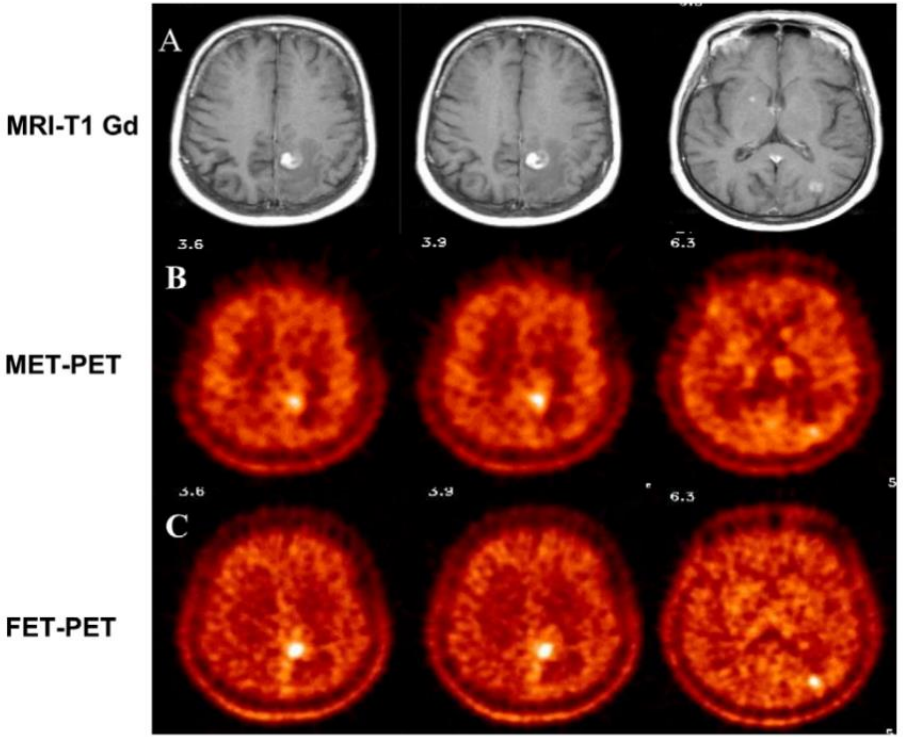
- **Hirnmetastasen**
- Meningeome
- Glomus Tumoren

Hirnmetastasen

Differenzierung zwischen Tumorprogress und Radionekrose nach RT





UNIVERSITÄTS KLINIKUM FREIBURG

Grosu et al. IJROBP 2011

Hirnmetastasen

Empfehlungen

Neuro-Oncology
21(5), 584–595, 2019 | doi:10.1093/neuonc/noz003 | Advance Access date 5 January 2019

PET imaging in patients with brain metastasis—report of the RANO/PET group

Norbert Galldiks, Karl-Josef Langen, Nathalie L. Albert, Marc Chamberlain, Riccardo Soffietti, Michelle M. Kim, Ian Law, Emilie Le Rhun, Susan Chang, Julian Schwarting, Stephanie E. Combs, Matthias Preusser, Peter Forsyth, Whitney Pope, Michael Weller, and Jörg C. Tonn

	Amino Acid PET (MET, FET, FDOPA)	FDG PET	Other PET Tracers	Oxford Level of Evidence
Identification of newly diagnosed BM	(++)	–	na	3
Differential diagnosis of newly diagnosed BM	(++)	–	na	3
Differentiation of radiation-induced changes from BM recurrence	++ *	+	na	2
Differentiation of immunotherapy-related changes from BM recurrence	(++)	na	na	3
Assessment of treatment response	(++)	na	(++)	3

++ high diagnostic accuracy; (++) high diagnostic accuracy, but limited data available; + limited diagnostic accuracy; – not helpful; na = only preliminary or no data available; *increased accuracy when using dynamic FET PET

Galldiks et al. Neuro-Oncol 2019

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Meningeome

AS-PET

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 2, pp. 339–344, 2006

0360-3016/06/$–see front matter

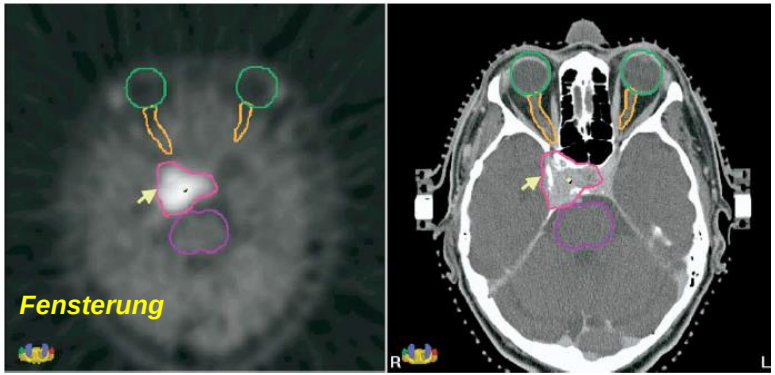
doi:10.1016/j.ijrobp.2006.02.047

CLINICAL INVESTIGATION **Brain**

^{11}C-METHIONINE PET IMPROVES THE TARGET VOLUME DELINEATION OF MENINGIOMAS TREATED WITH STEREOTACTIC FRACTIONATED RADIOTHERAPY

Anca-Ligia Grosu, M.D.,* Wolfgang A. Weber, M.D.,†‡ Sabrina T. Astner, M.D.,* Markus Adam, M.D.,* Bernd J. Krause, M.D.,† Markus Schwaiger, M.D.,† Michael Molls, M.D.,* and Carsten Nieder, M.D.*

Departments of *Radiation Oncology and †Nuclear Medicine, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; ‡Department of Molecular and Medical Pharmacology, UCLA David Geffen School of Medicine, Los Angeles, CA



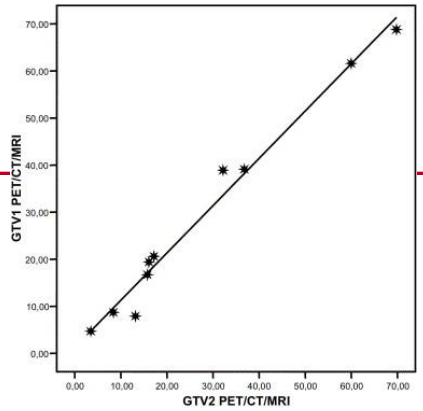
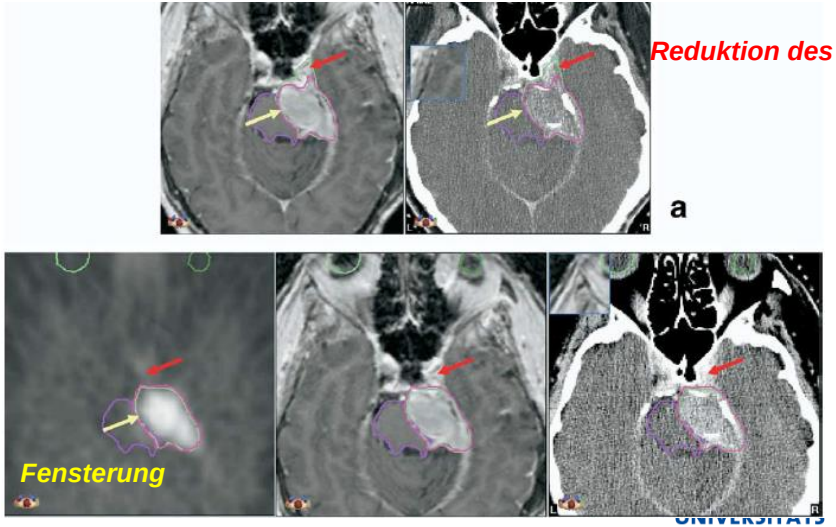


Table 2. Individual patient data for CT/MRI/PET-based planning target volume definition

Patient no.	GTV-B Observer 1 (cm^3)	GTV-B Observer 2 (cm^3)	GTV changes when PET was added to CT/MRI
1	19.4	16.1	Reduction, both observers
2	16.8	15.8	Discordant changes
3	4.8	3.8	Discordant changes
4	69.2	70.2	Reduction, both observers
5	8.9	8.7	Reduction, both observers
6	62.3	61.1	Reduction, both observers
7	39.5	32.7	Increase, both observers
8	20.9	17.3	Discordant changes
9	39.4	37.1	Increase, both observers
10	8.1	13.4	Discordant changes

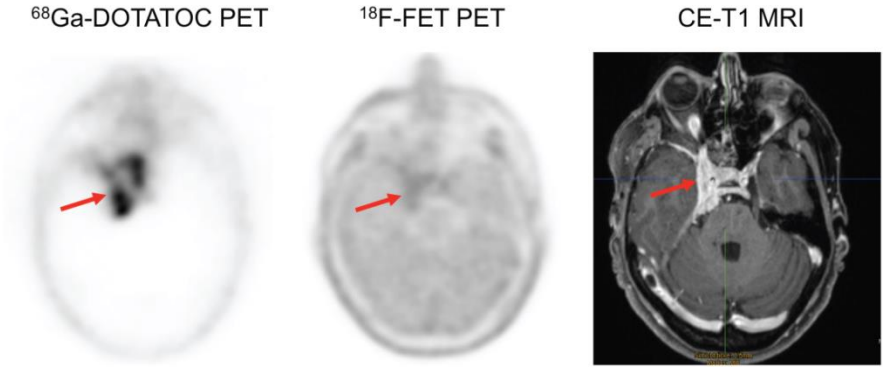


UNIVERSITÄTS KLINIKUM FREIBURG

Grosu et al. IJROBP 2006

Meningeome

PET mit SSTR Liganden



DOTATOC **DOTATATE**

DOTANOC

1576 Neuro-Oncology
19(12), 1576–1587, 2017 | doi:10.1093/neuonc/nox112 | Advance Access date 12 June 2017

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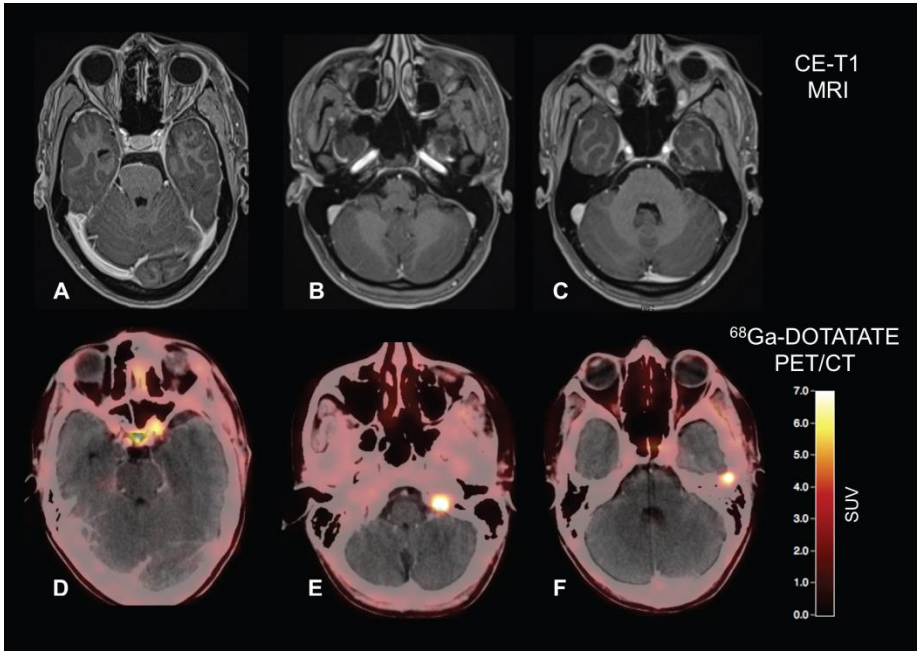

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Meningeome

Empfehlungen

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Clinical Indication	PET Ligands for Somatostatin Receptors	Amino Acid PET Tracers	Other PET Tracers
Detection of meningioma tissue/ differential diagnosis	^{68}Ga-DOTATOC and ^{68}Ga-DOTATATE PET may add valuable diagnostic information[24,53]	na	na
Meningioma grading	^{68}Ga-DOTATATE binding correlates with tumor growth rate in WHO grades I and II meningiomas[35]	^{11}C-MET correlates with proliferative activity,[54] but data on grading are controversial.[34,55] Static and dynamic ^{18}F-FET PET may provide additional information for meningioma grading[32]	^{11}C-choline seems to be helpful for meningioma grading.[41] ^{11}C-acetate seems not to be helpful[18]
Delineation of tumor extent for resection planning	^{68}Ga-DOTATATE PET delineates the meningioma extent better than standard MRI[23,61]	na	na
Delineation of tumor extent for radiation treatment planning	^{68}Ga-DOTATOC PET delivers additional information on tumor extent for radiotherapy target definition[56,57,64,65]	^{11}C-MET PET significantly influences GTV delineation in meningiomas[31,59]	na
Treatment monitoring	na	^{11}C-MET PET allows an earlier evaluation of treatment effects than standard imaging.[66,67] Boronated amino acid PET probes may help to evaluate treatment effects[38]	na
Diagnosis of tumor progression/differentiation of tumor progression from posttreatment changes	^{68}Ga-DOTATOC/^{68}Ga-DOTATATE PET is useful for differentiation between progression and posttreatment changes[23,24,52]	na	na

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Inhalt

- Gliome
- Hirnmetastasen
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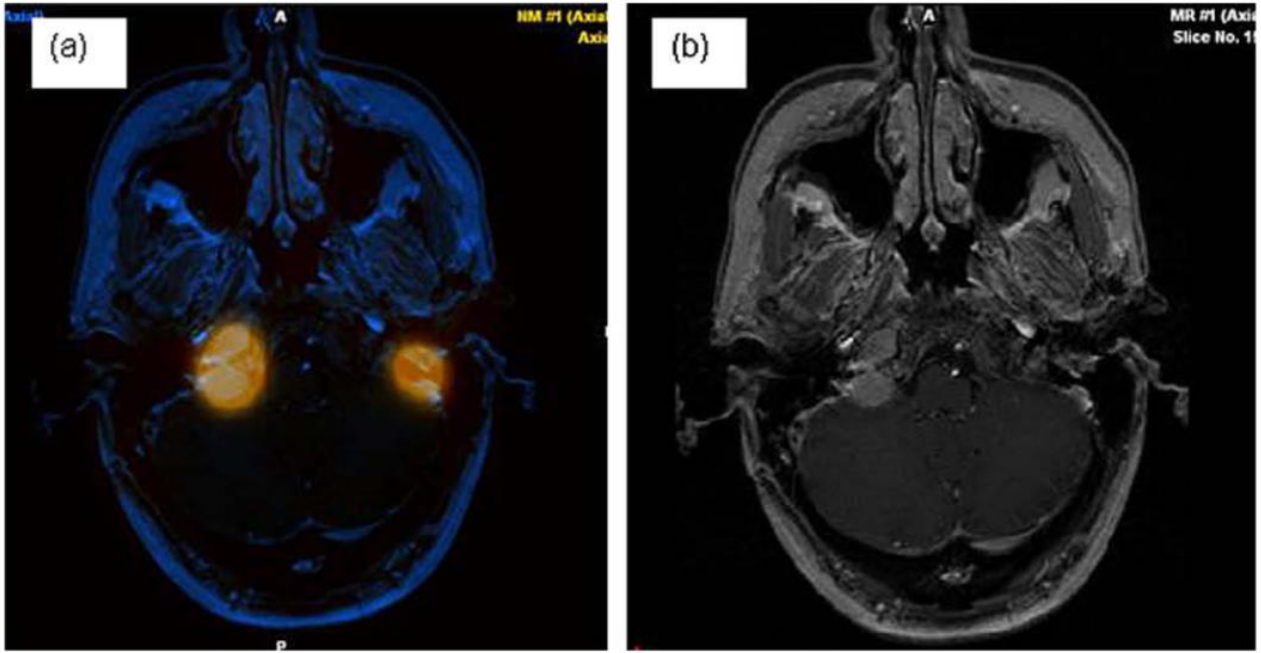
Glomus Tumoren

PET mit SSTR Liganden



Astner et al. IJROBP 2008

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Vielen Dank!