

Vorlesung Nuklearmedizin in der Medizinphysik

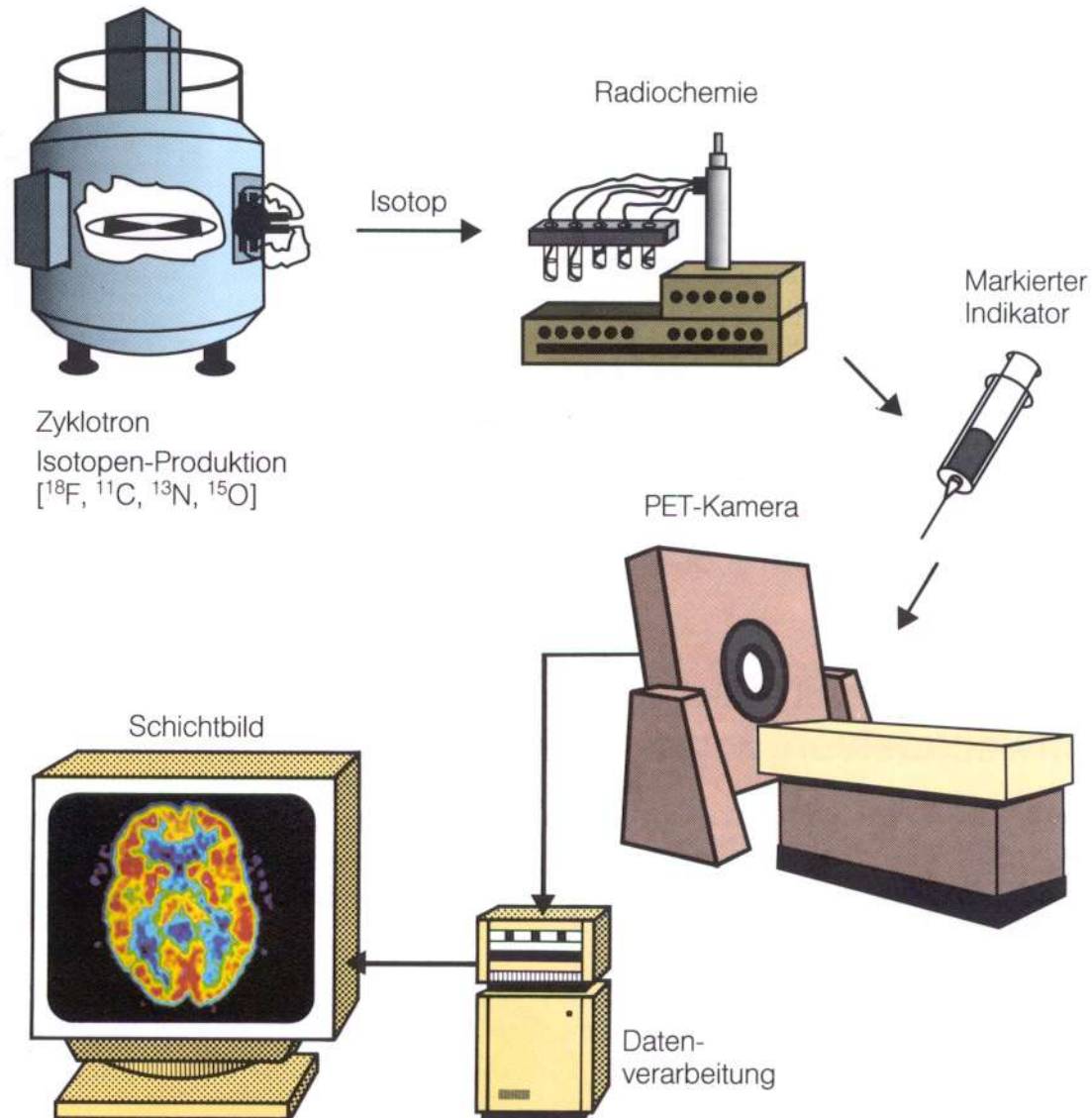
Einsatz der Positronen-Emissions-Tomographie

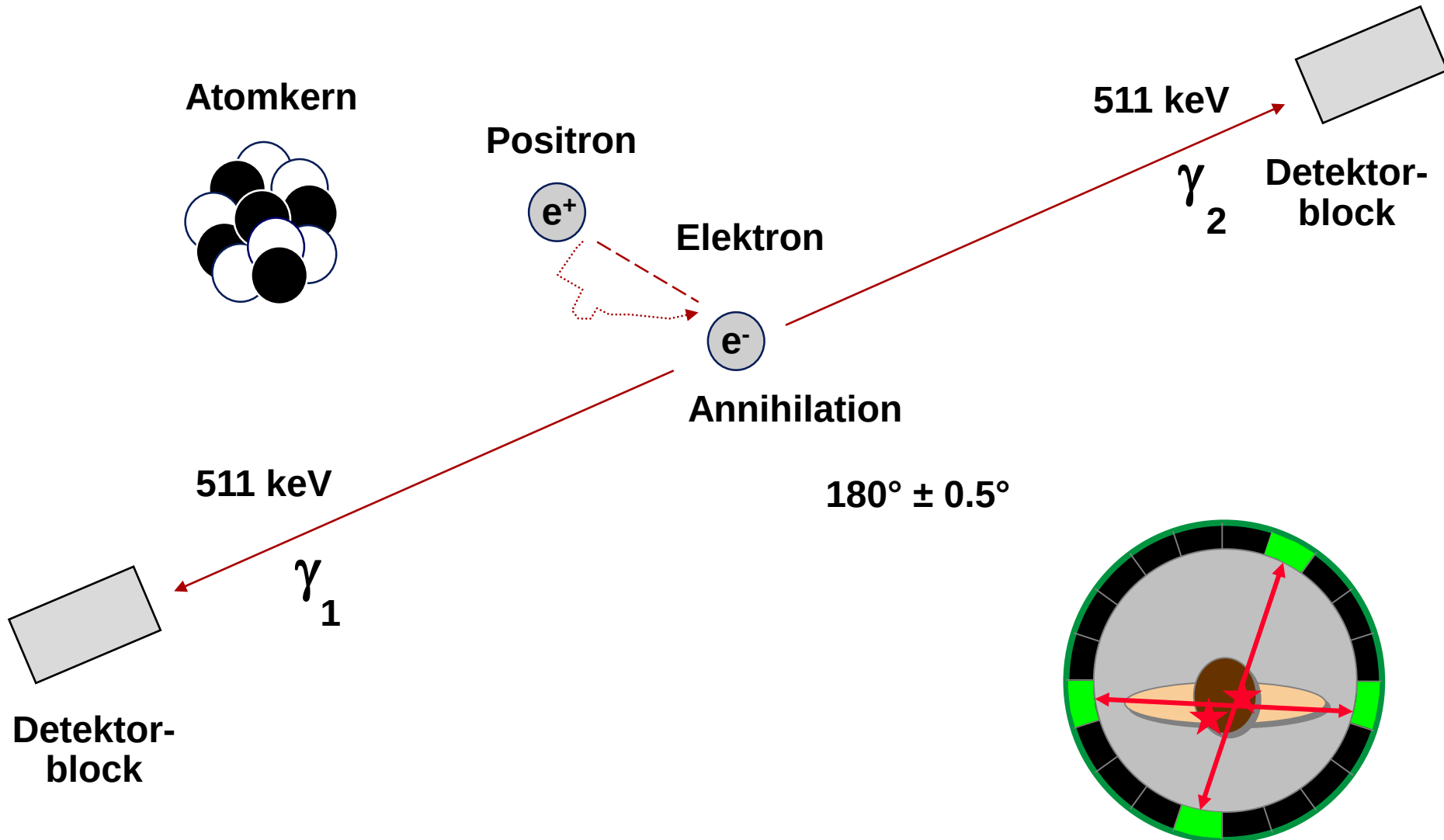
Prof. Dr. Christian la Fougère



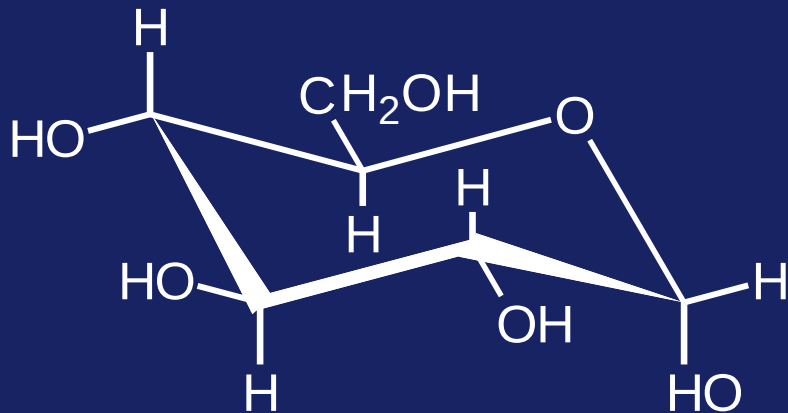


- Methode mit der biochemische und physiologische Vorgänge im menschlichen Körper von außen erfasst werden können
- Verwendung von Radio-Tracer-Methoden mit Bildrekonstruktionsverfahren gestattet es, die regionalen Stoffwechselveränderungen in 3 D darzustellen
- Markierung mit Positronenstrahlern erlaubt eine Quantifizierung der im Organismus ablaufenden Prozesse

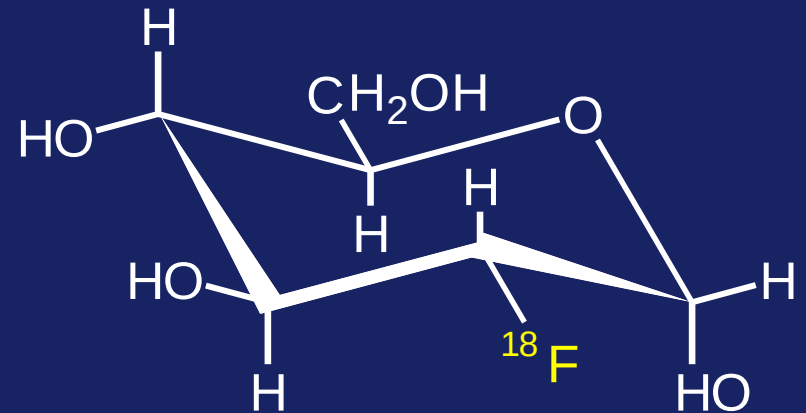




Nuklid	Halbwertszeit	Beispiel	Funktion
C-11	20.4 min	Methionin	AS-Metab.
C-11	20.4 min	Raclopride	D2 Rezeptoren
N-13	9.96 min	NH ₃	Perfusion
O-15	2.05 min	H ₂ O	Perfusion
F-18	109.7 min	FDG	Glukose-Metabolismus
F-18	109.7 min	FET	AS-Metabolismus
F-18	109.7 min	F-DOPA	Neurotransmitter
F-18	109.7 min	FLT	Proliferationsmarker
Ga-68	67.7 min	DOTA-TATE	Somatostatin-Rezeptor



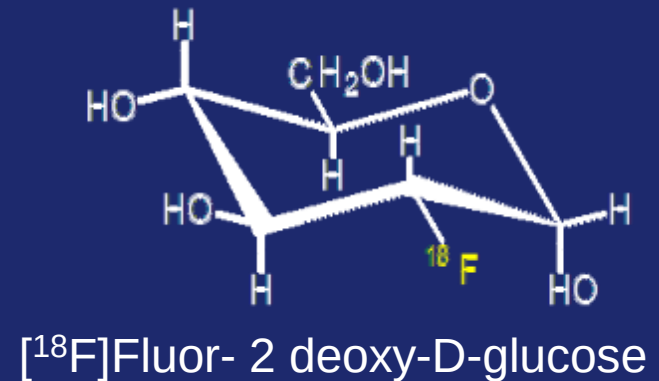
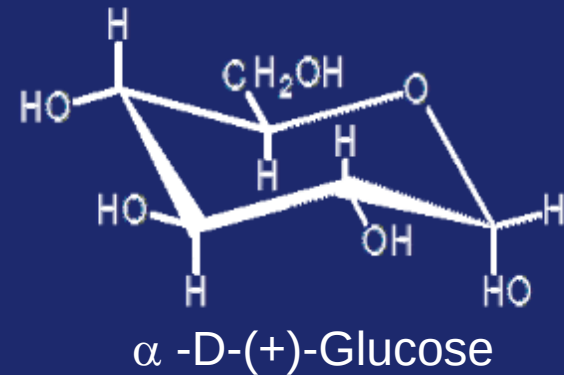
α -D-(+)-Glucose



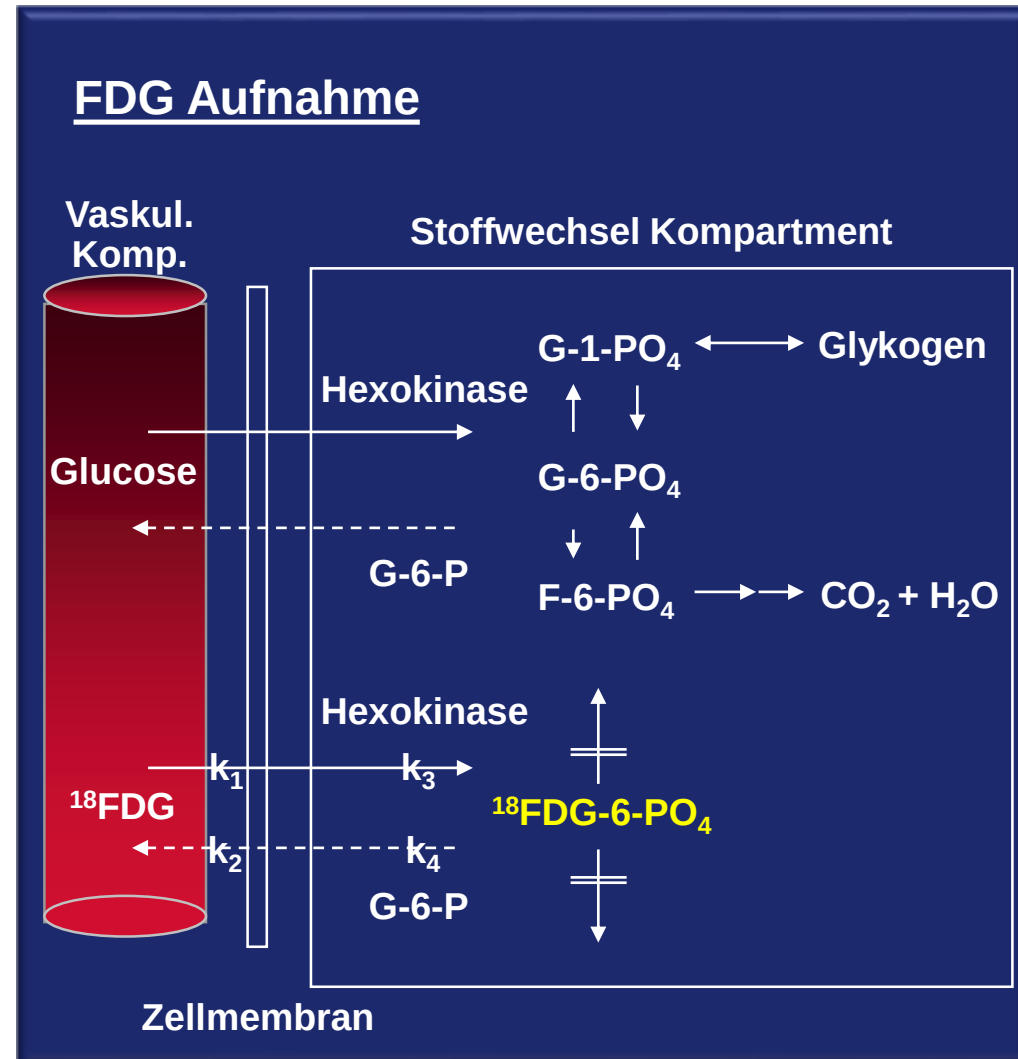
2-(^{18}F)Fluor-2-deoxy-D-glucose
 ^{18}F -FDG

- $[^{18}\text{F}]$ FDG wird analog zu Glucose in Tumorzellen aufgenommen
- Tumorzellen nehmen vermehrt Glucose auf
- erhöhte Zahl von Glucose-Transporter Molekülen (GLUT1 - GLUT5)
- gesteigerte Glykolyse

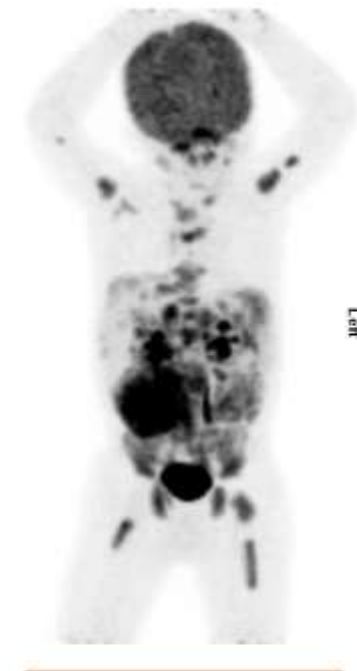
Radiopharmakon



- [^{18}F]-FDG –Uptake und biologischen Eigenschaften von Tumoren:
 - Histologisches Grading
 - Proliferative Aktivität
 - Anzahl vitaler Tumorzellen
 - Gewebeoxygenierung
 - regionale Perfusion
 - peritumorale Entzündungsreaktion

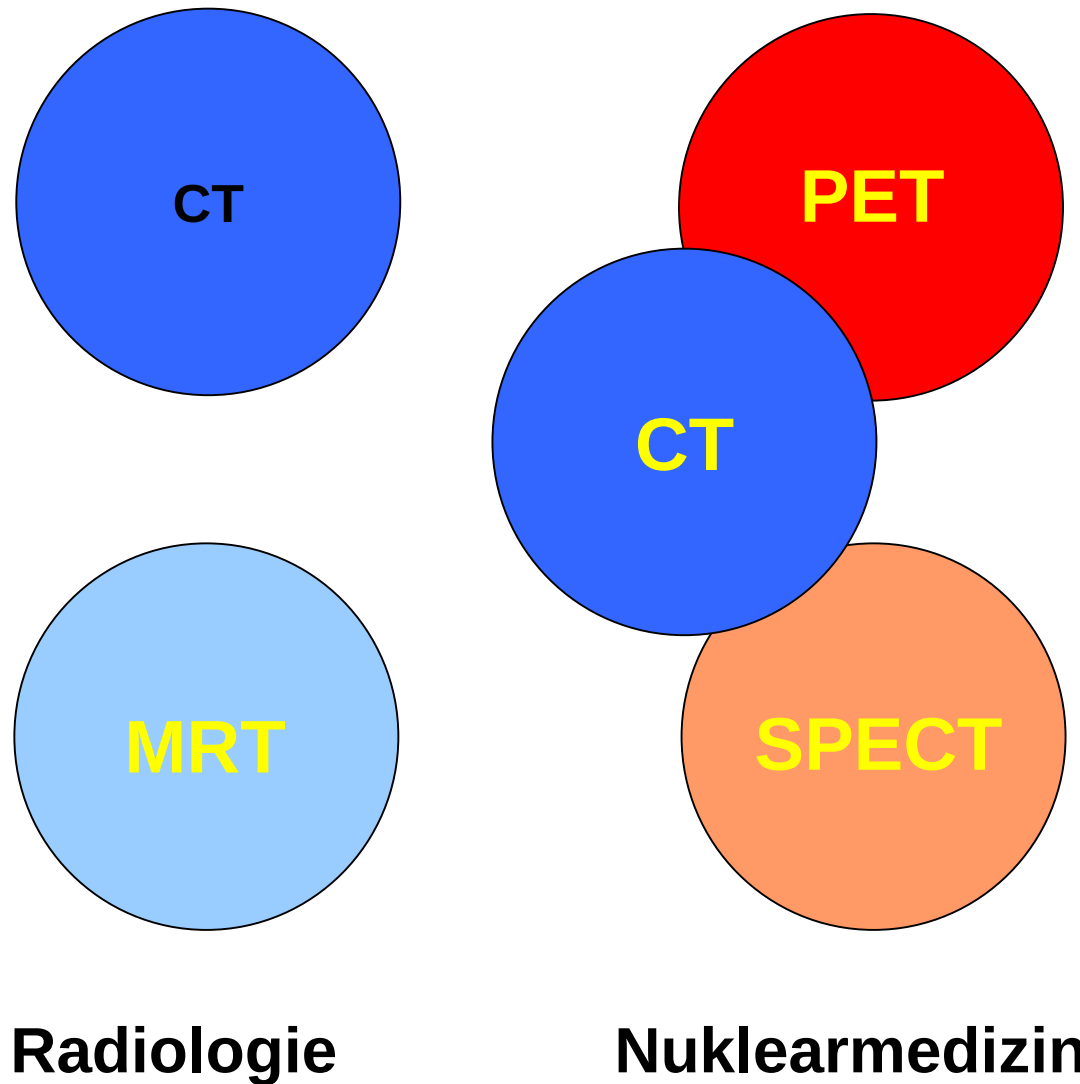


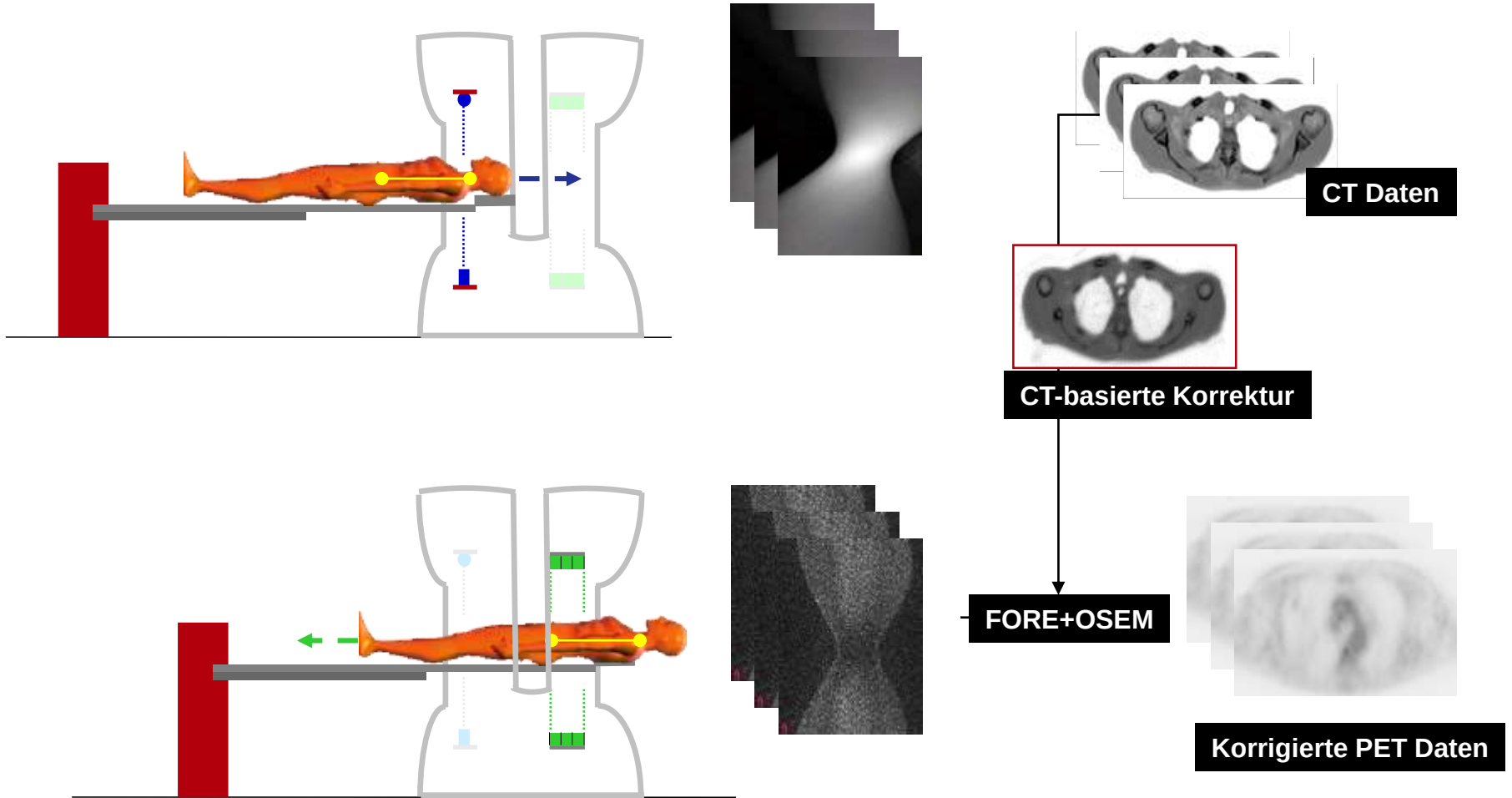
- Onkologie
- Neurologie
- Kardiologie
- Entzündungsdiagnostik



HERMES

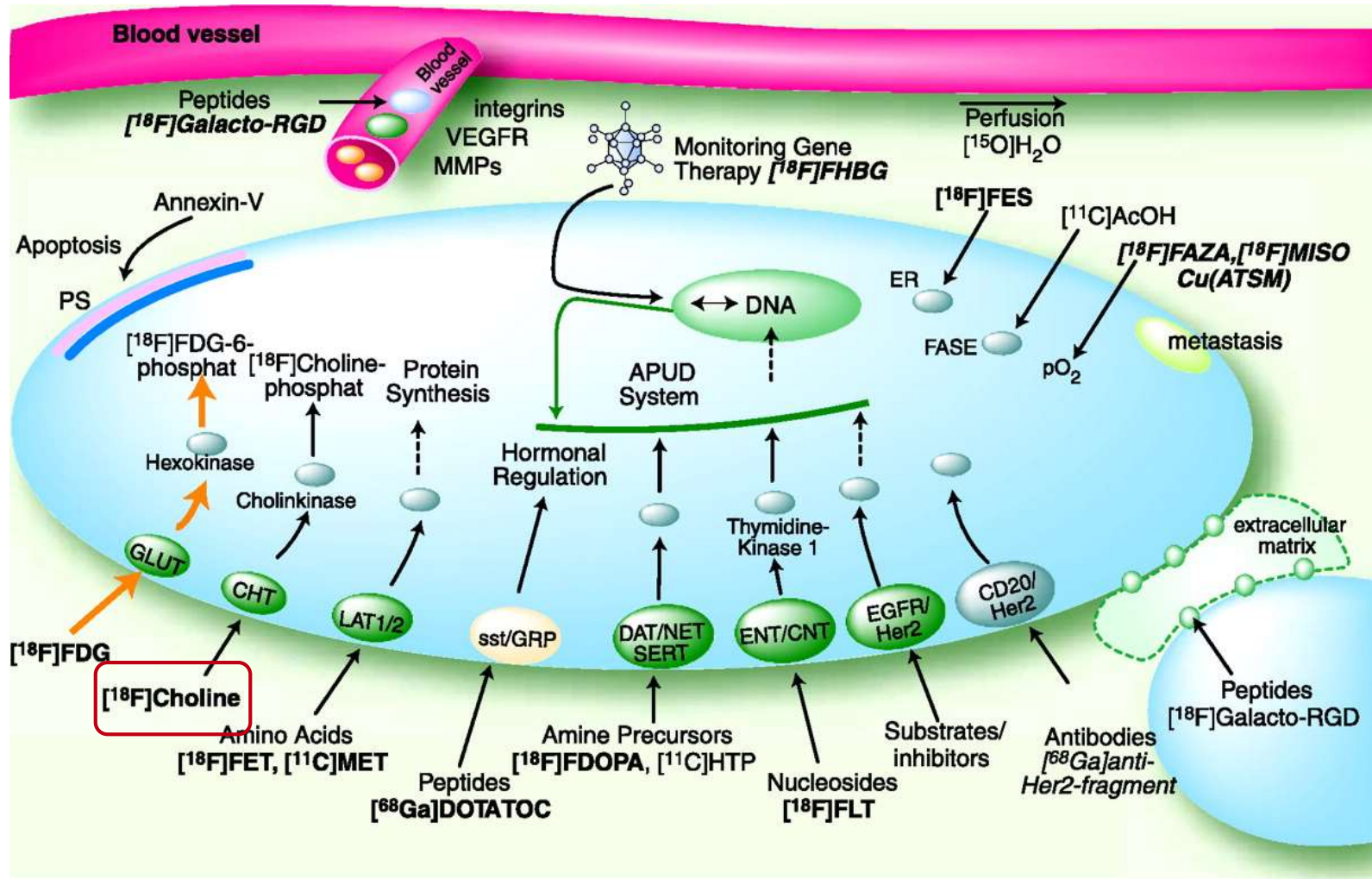






	effektive Dosis (mSv)	
Topogramm	< 0,1	
low-dose CT (Transmission)	4,5	
PET (300 MBq FDG)	5,7	3,8 (200 MBq)
Ganzkörper CT (diagnostisch)	14,1	
gesamt	24,4	22,5

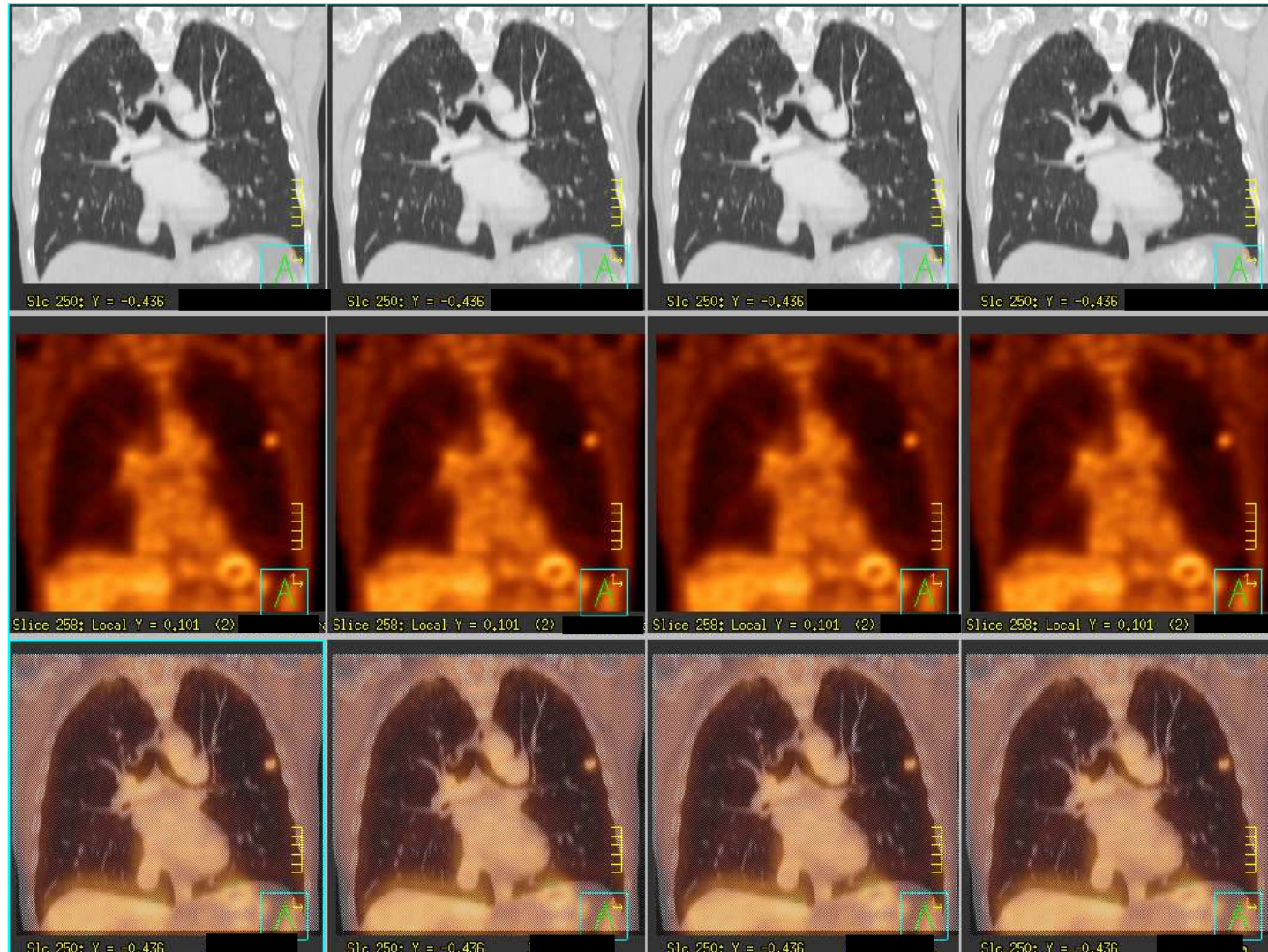
(G. Brix et al., BfS)

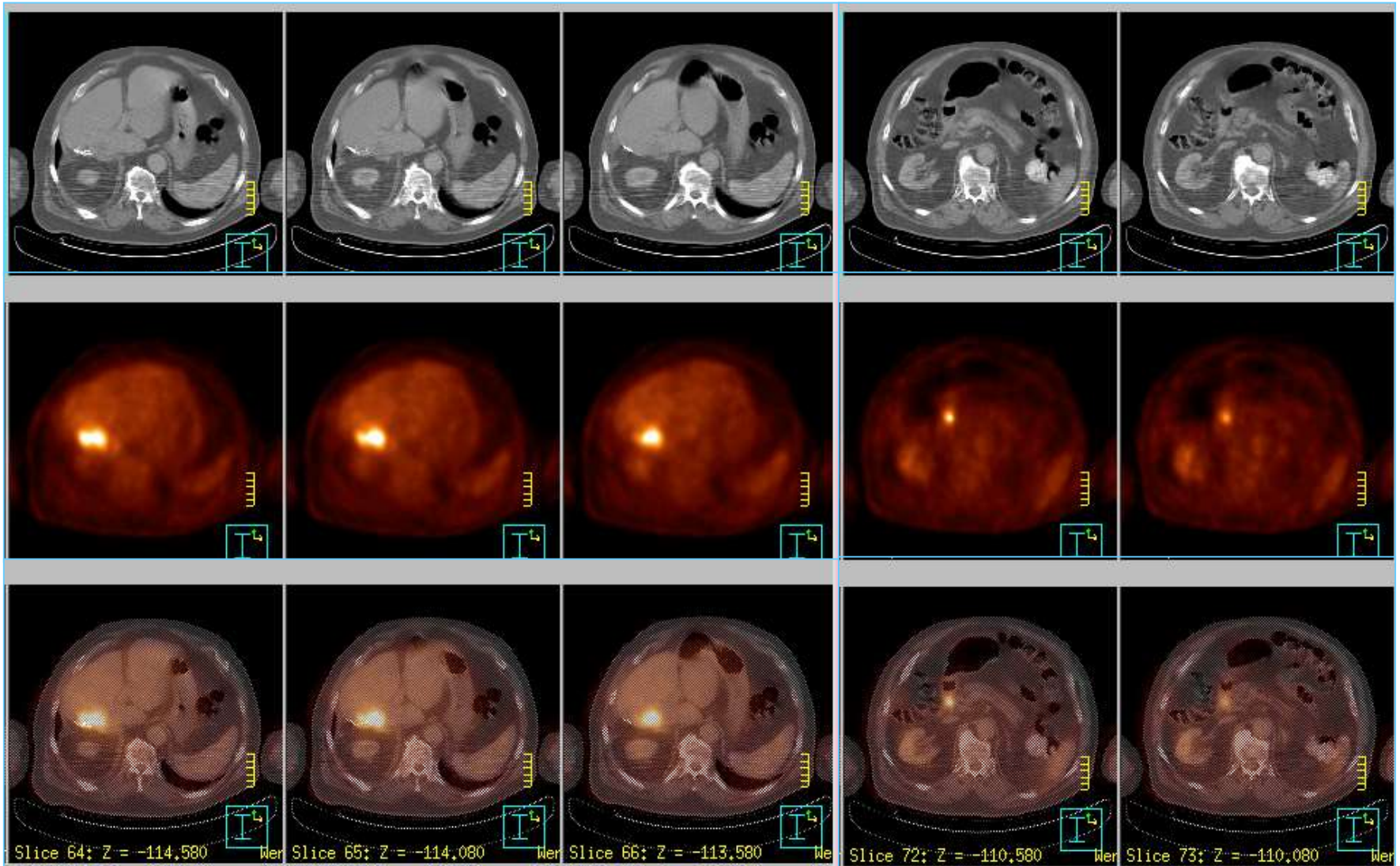


- Primärtumordiagnostik
- Staging
- Therapieplanung
- Therapiemonitoring
- DD Narbe – Rezidiv, Restaging



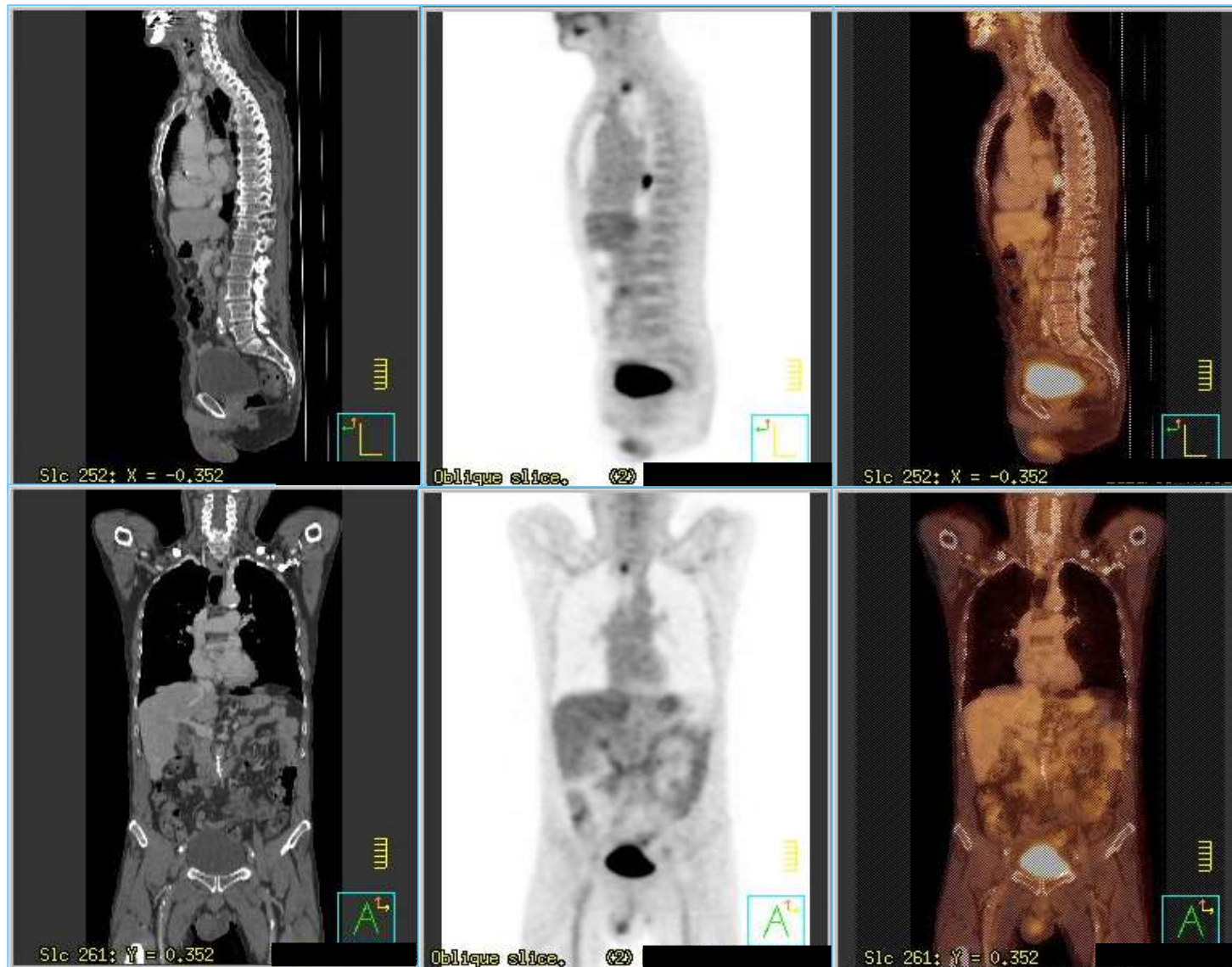


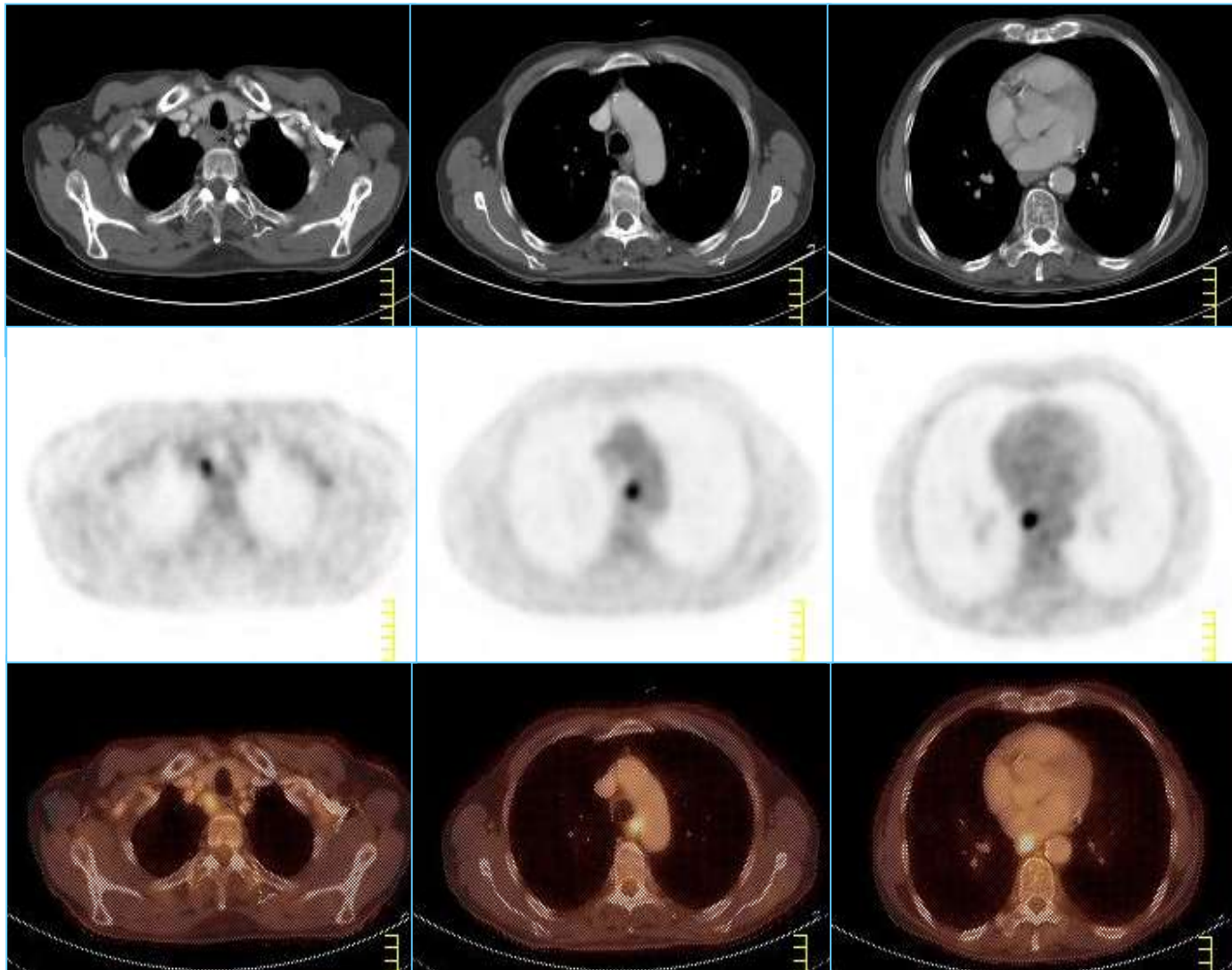




Kolonkarzinom und Leberfilia

Fallbeispiel: 55-jähriger Patient, unklarer Gewichtsverlust

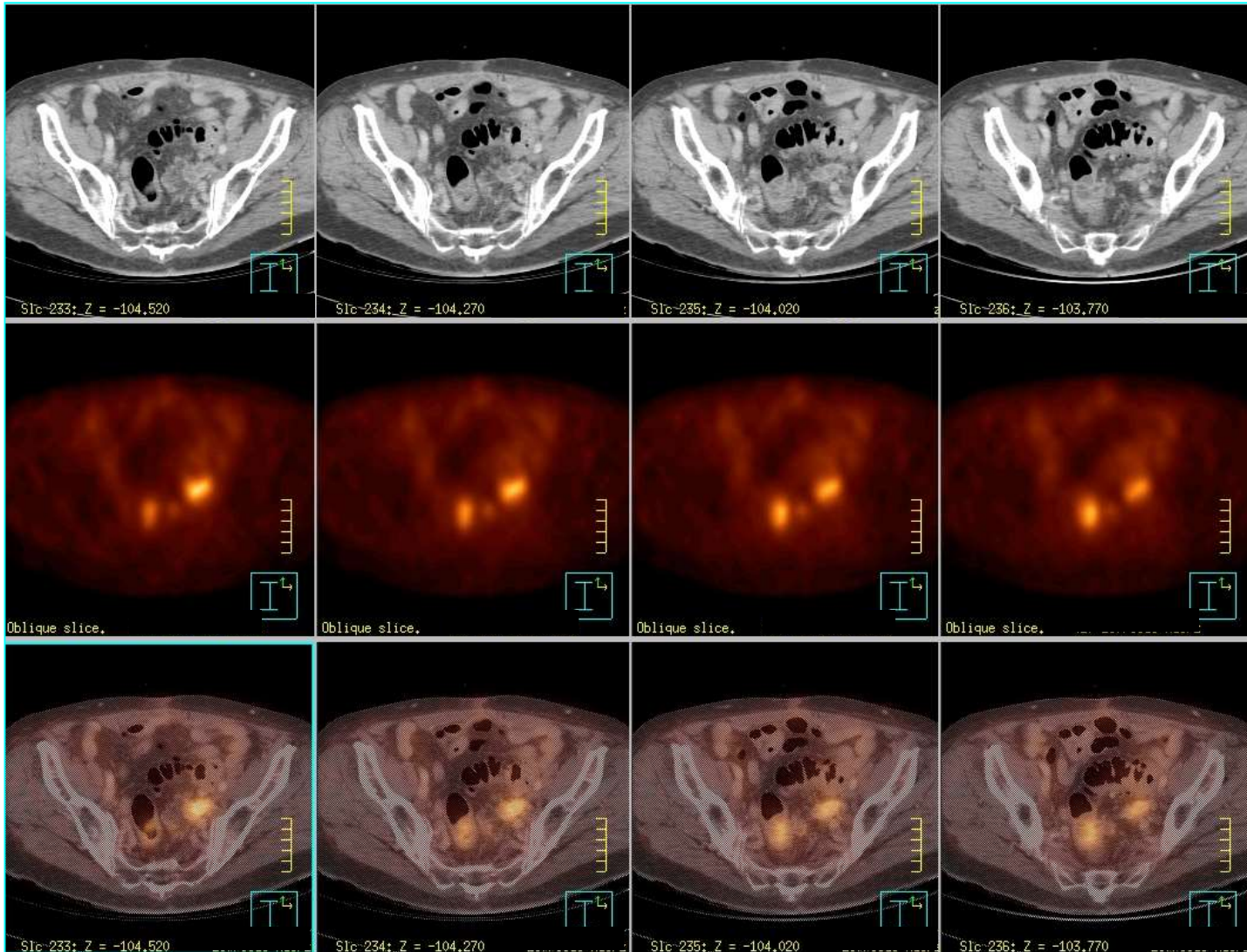


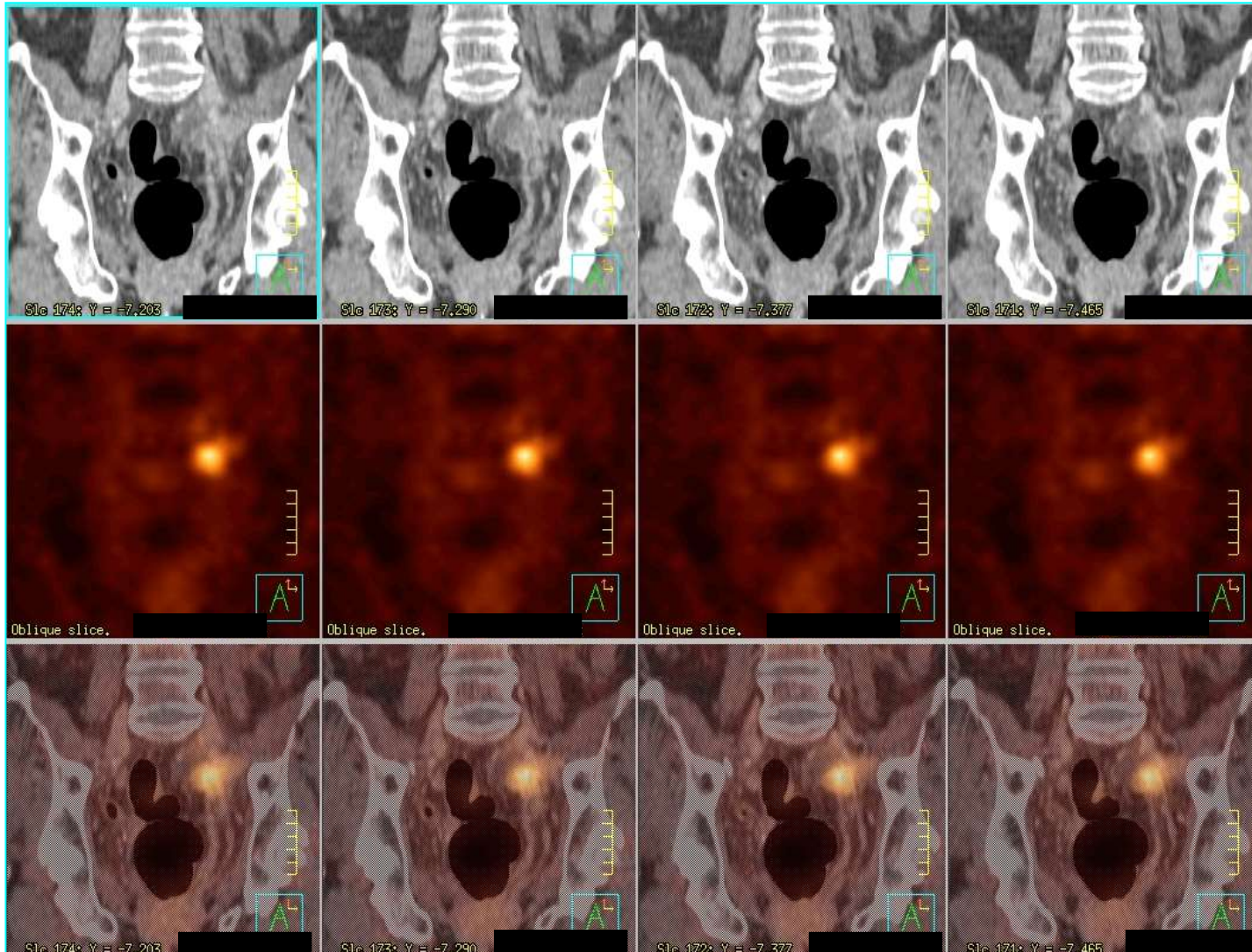


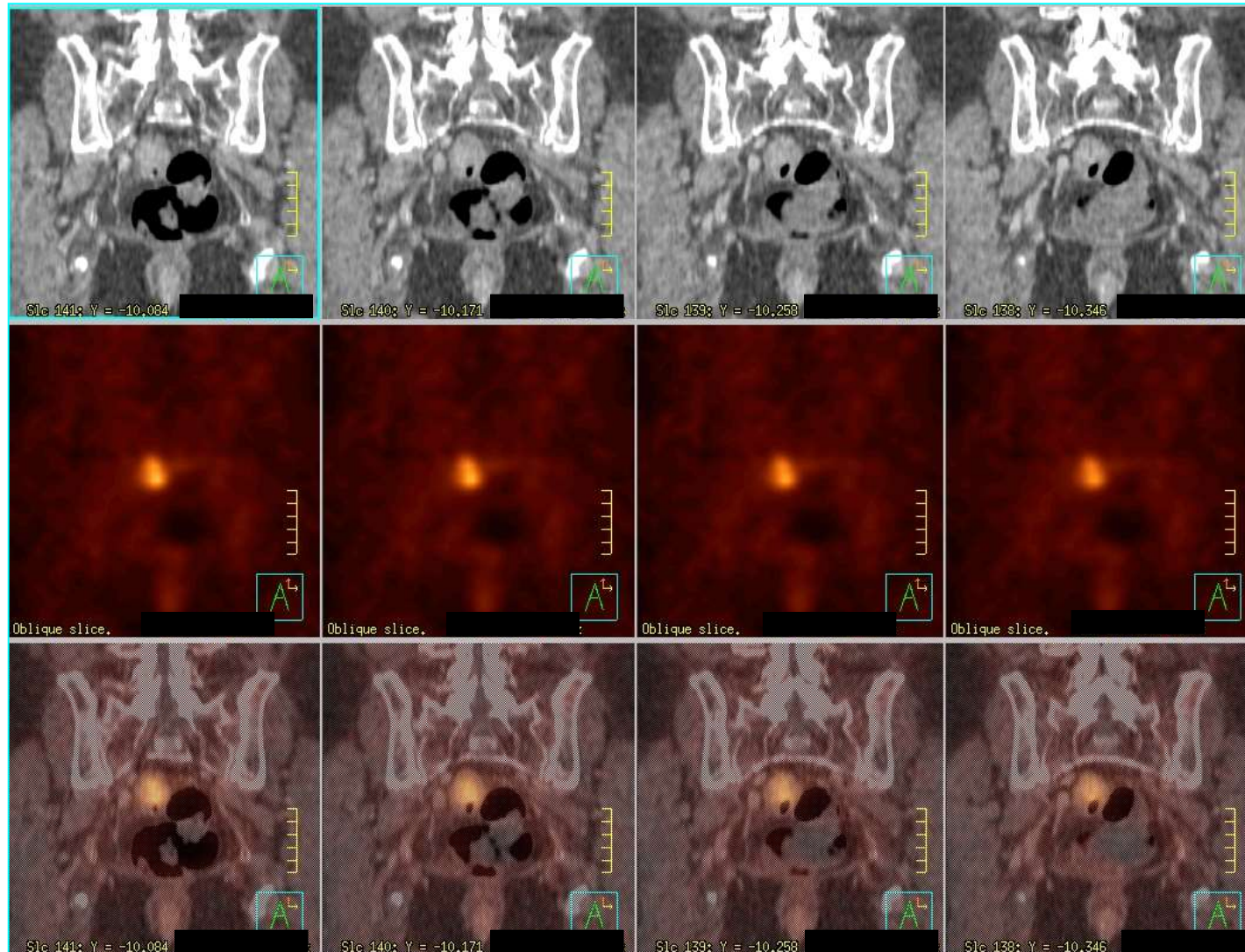
Ösophagus-Ca + LK-Metastasen

- ✓ Primärtumordiagnostik
- Staging
- Therapieplanung
- Therapiemonitoring
- DD Narbe – Rezidiv, Restaging

Fallbeispiel: 78-jährige Patientin, Endometriumkarzinom

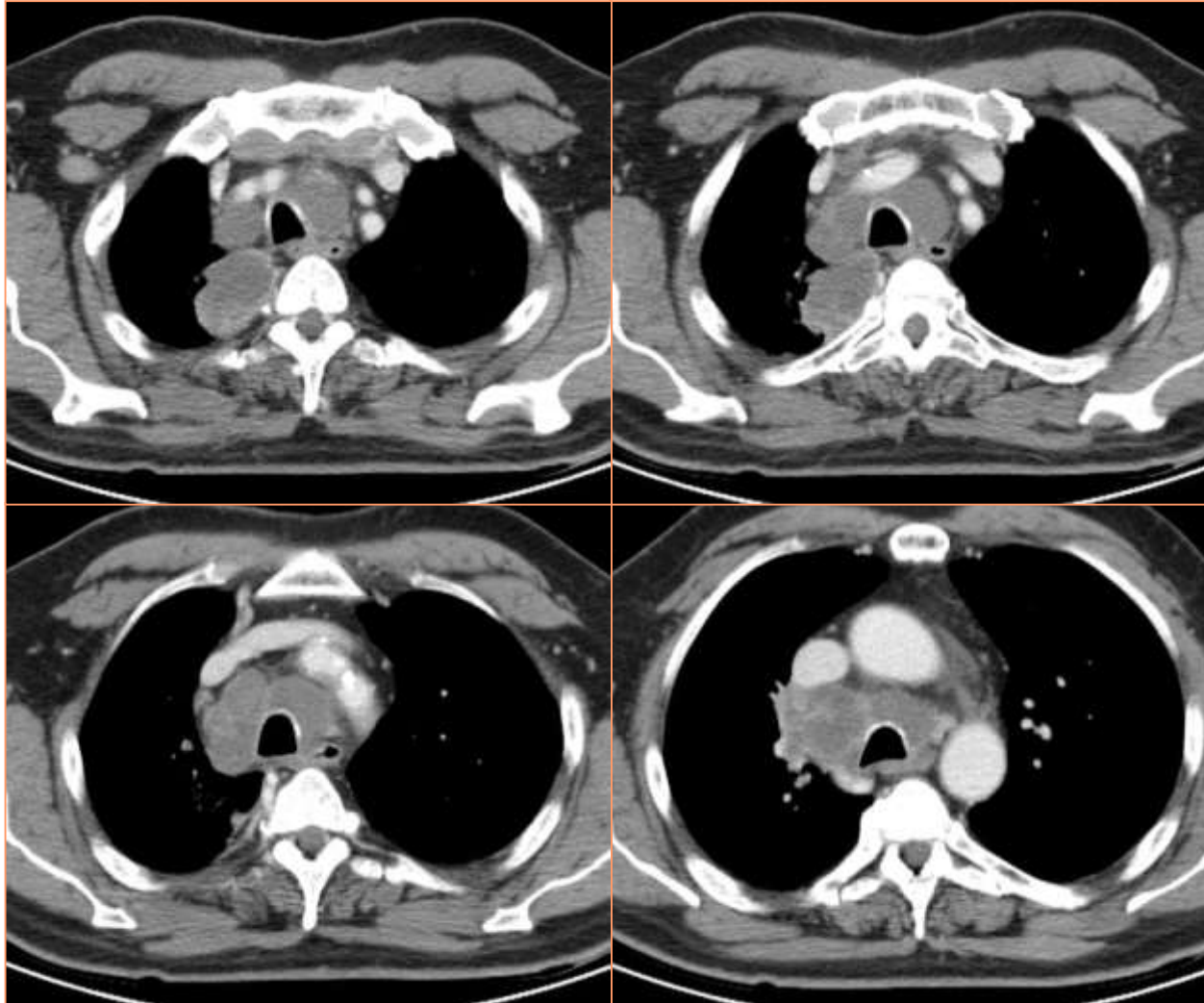




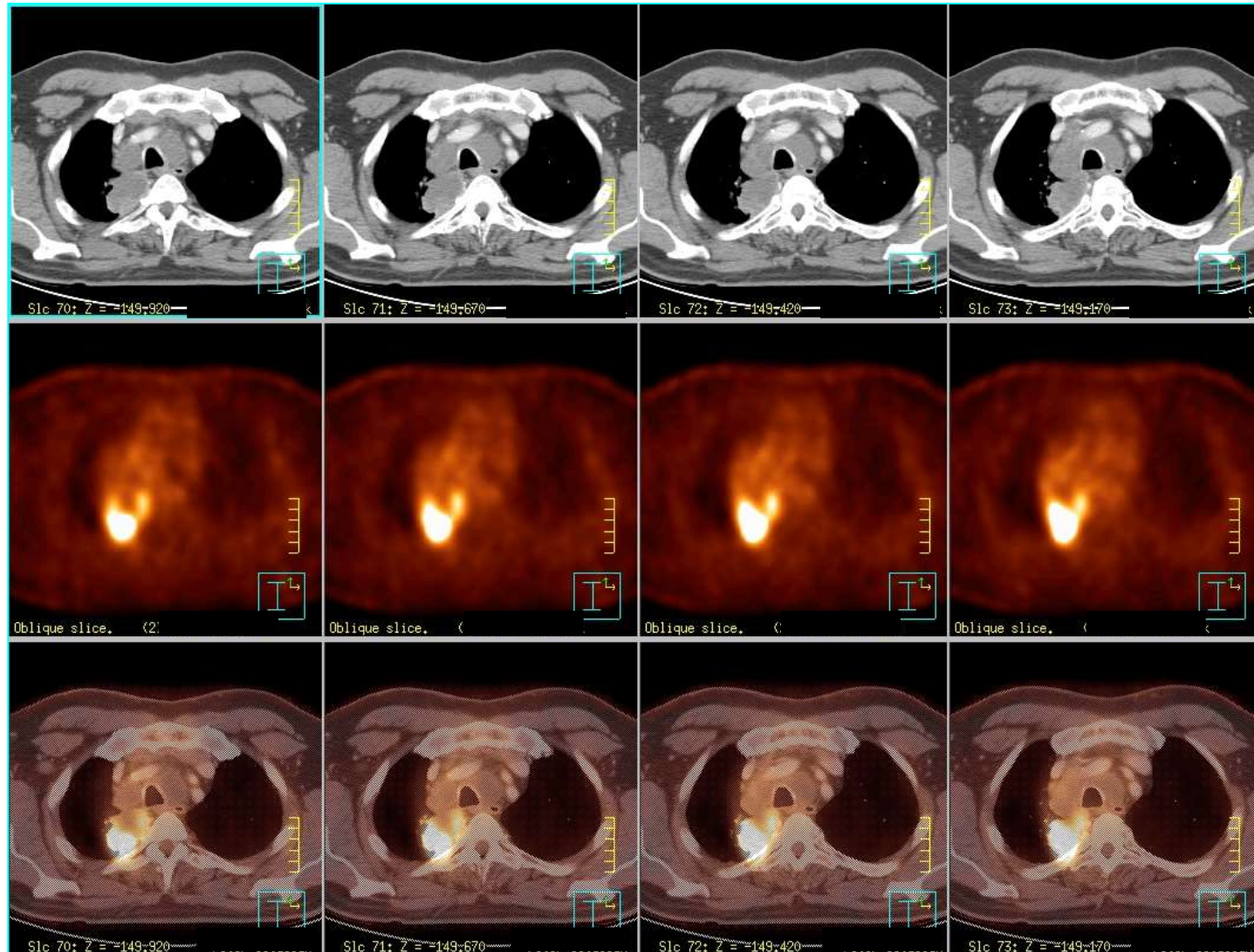


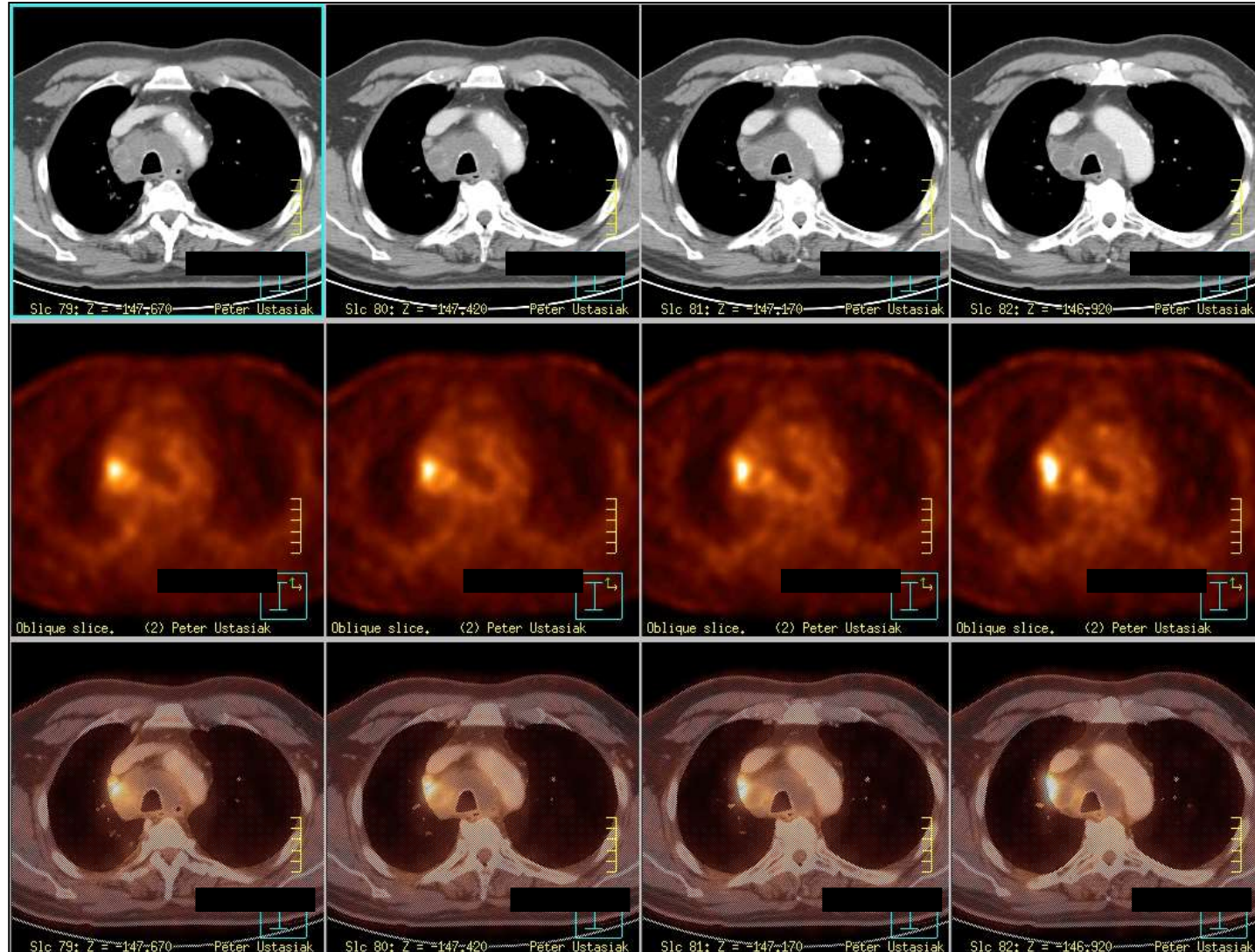
2 Darmwandmetastasen

- ✓ Primärtumordiagnostik
- ✓ Staging
 - Therapieplanung
 - Therapiemonitoring
 - DD Narbe – Rezidiv, Restaging



Histologisch (Mediastinoskopie) kein Malignomnachweis



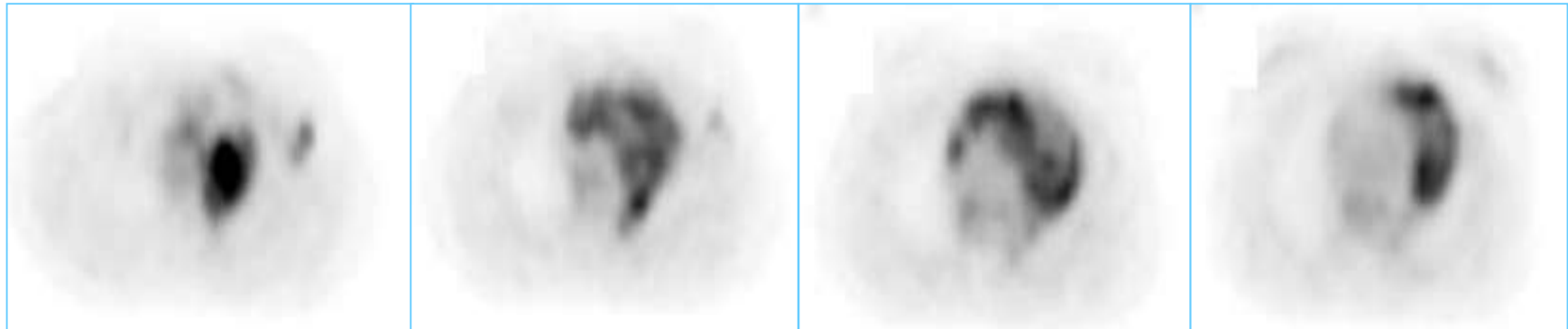
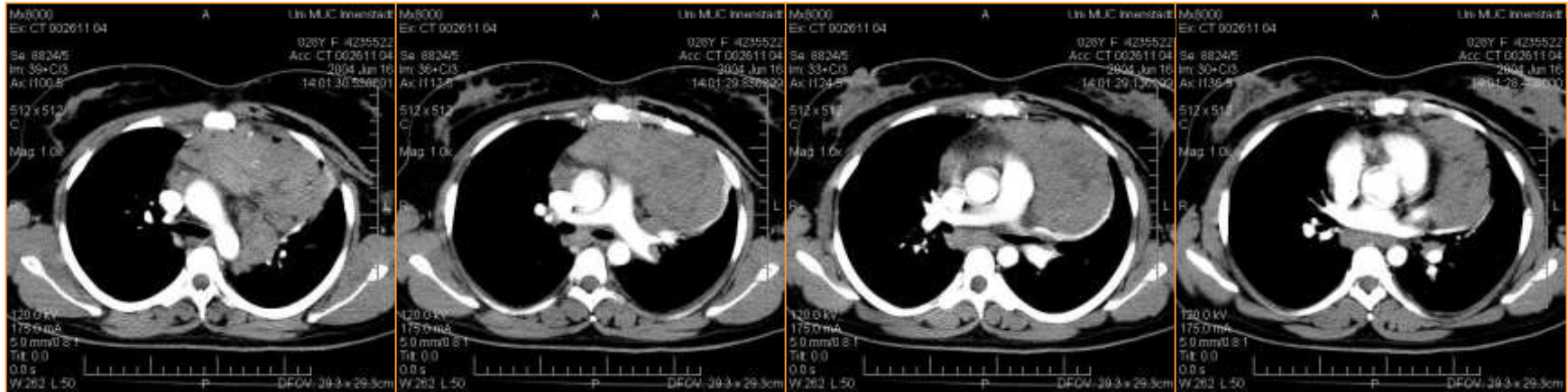


Nochmalige Endoskopie: Metastasiertes Bronchialkarzinom

- ✓ Primärtumordiagnostik
- ✓ Staging
- ✓ Therapieplanung
 - Therapiemonitoring
 - DD Narbe – Rezidiv, Restaging



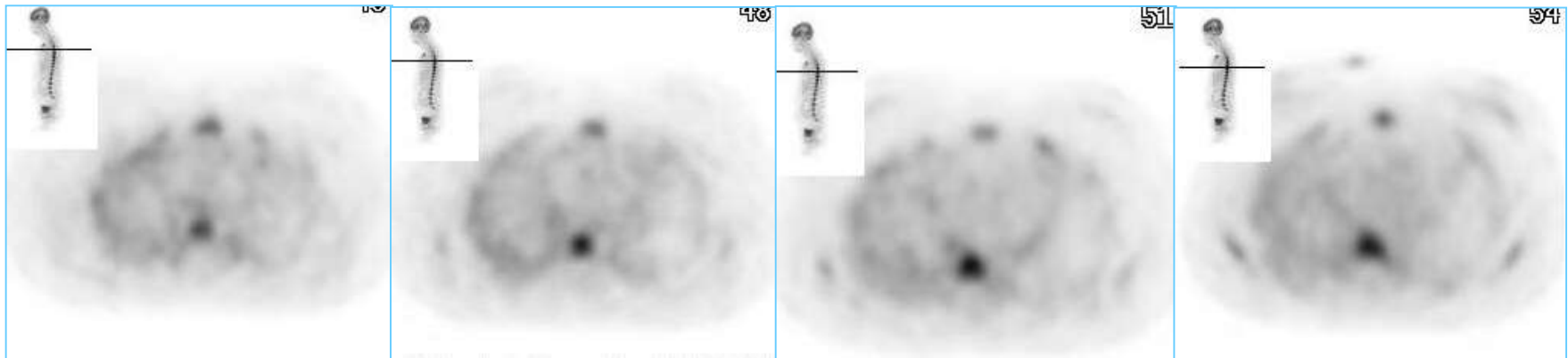
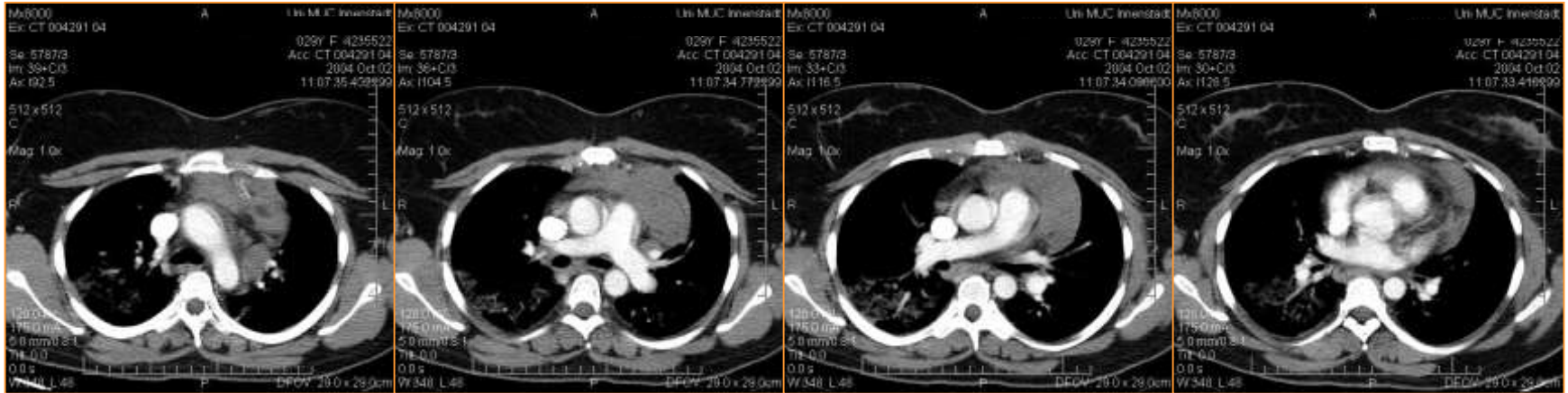
prätherapeutisch (6/04)



prätherapeutisch (6/04)



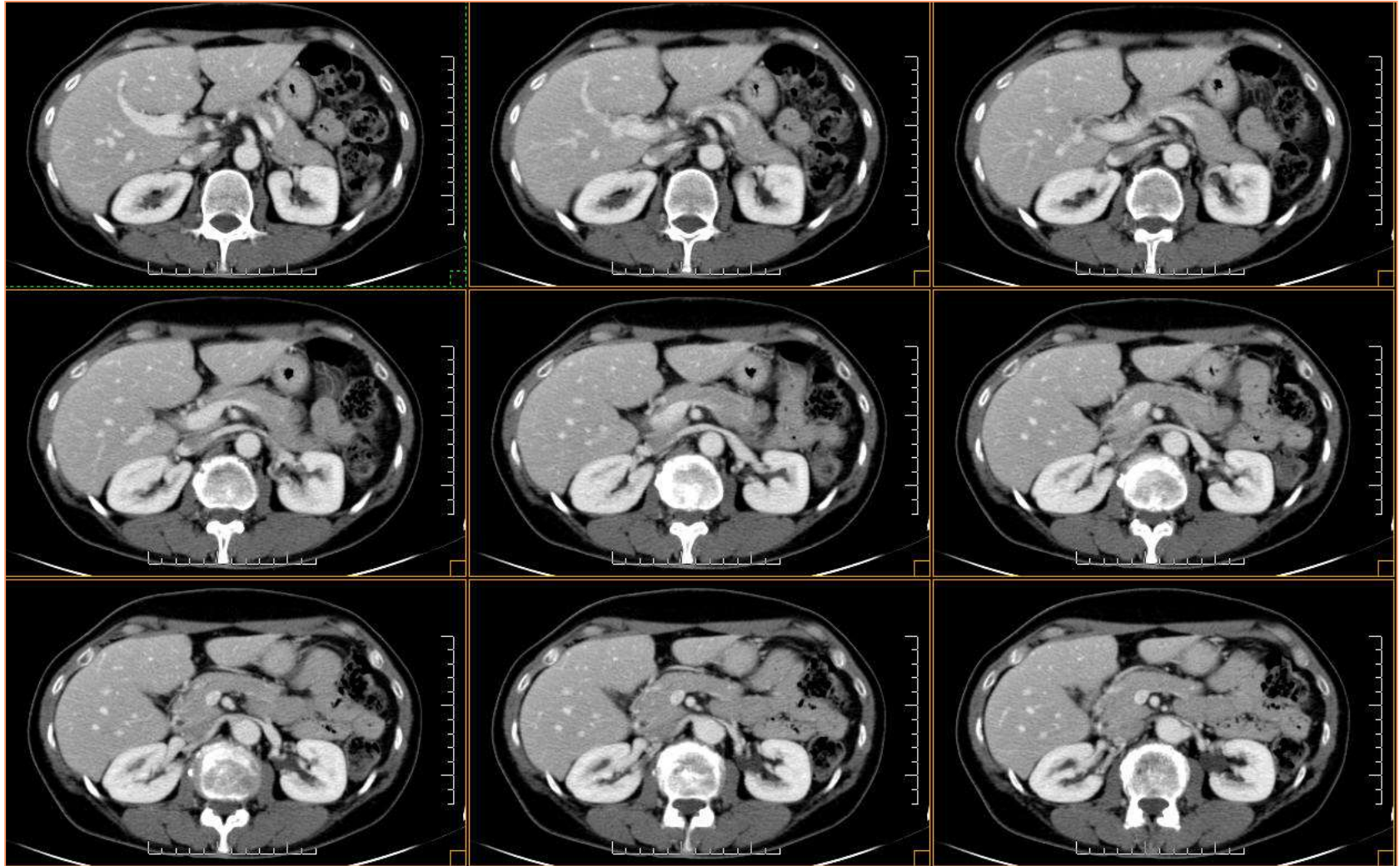
nach 4 Zyklen Chemotherapie (9/04)

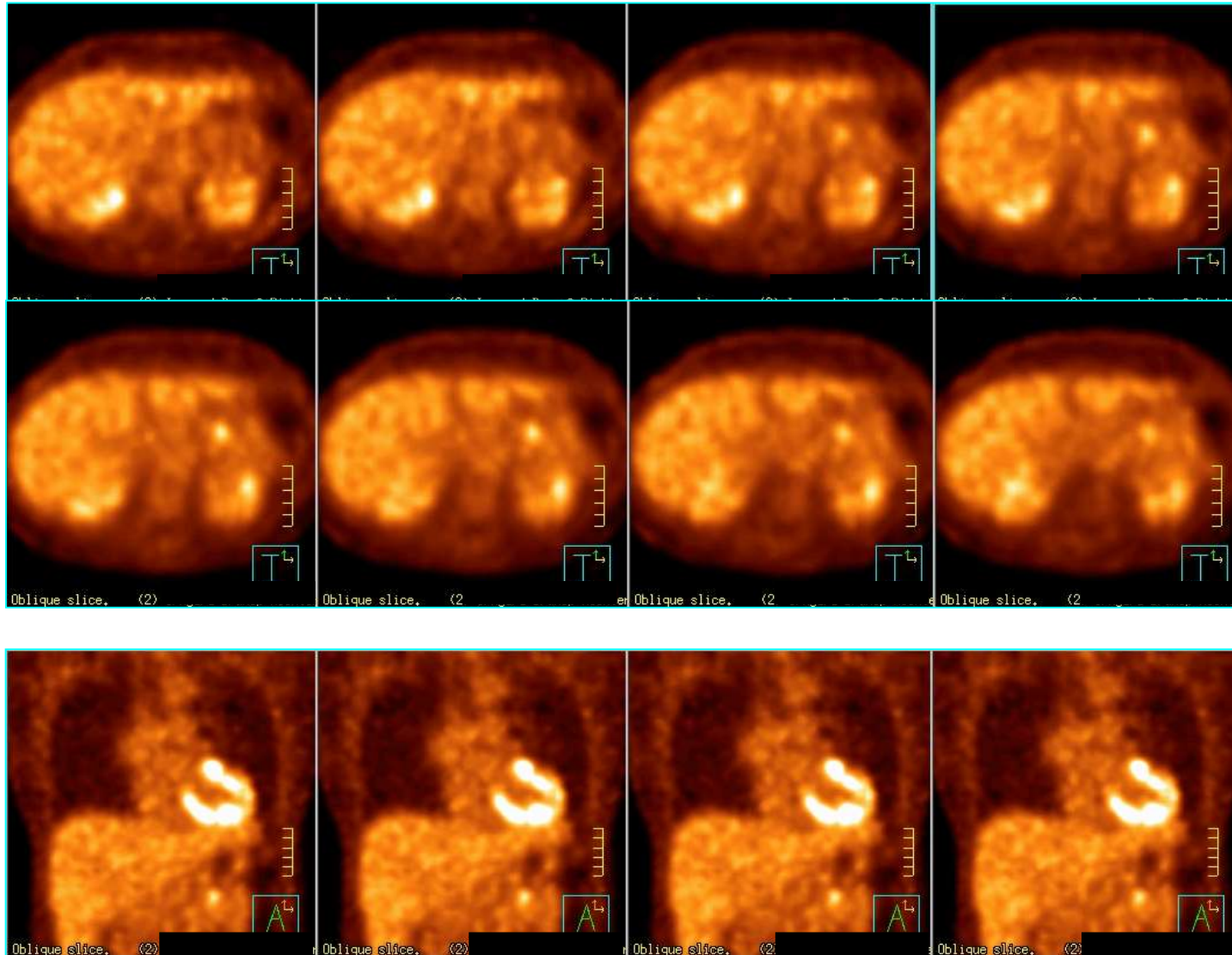


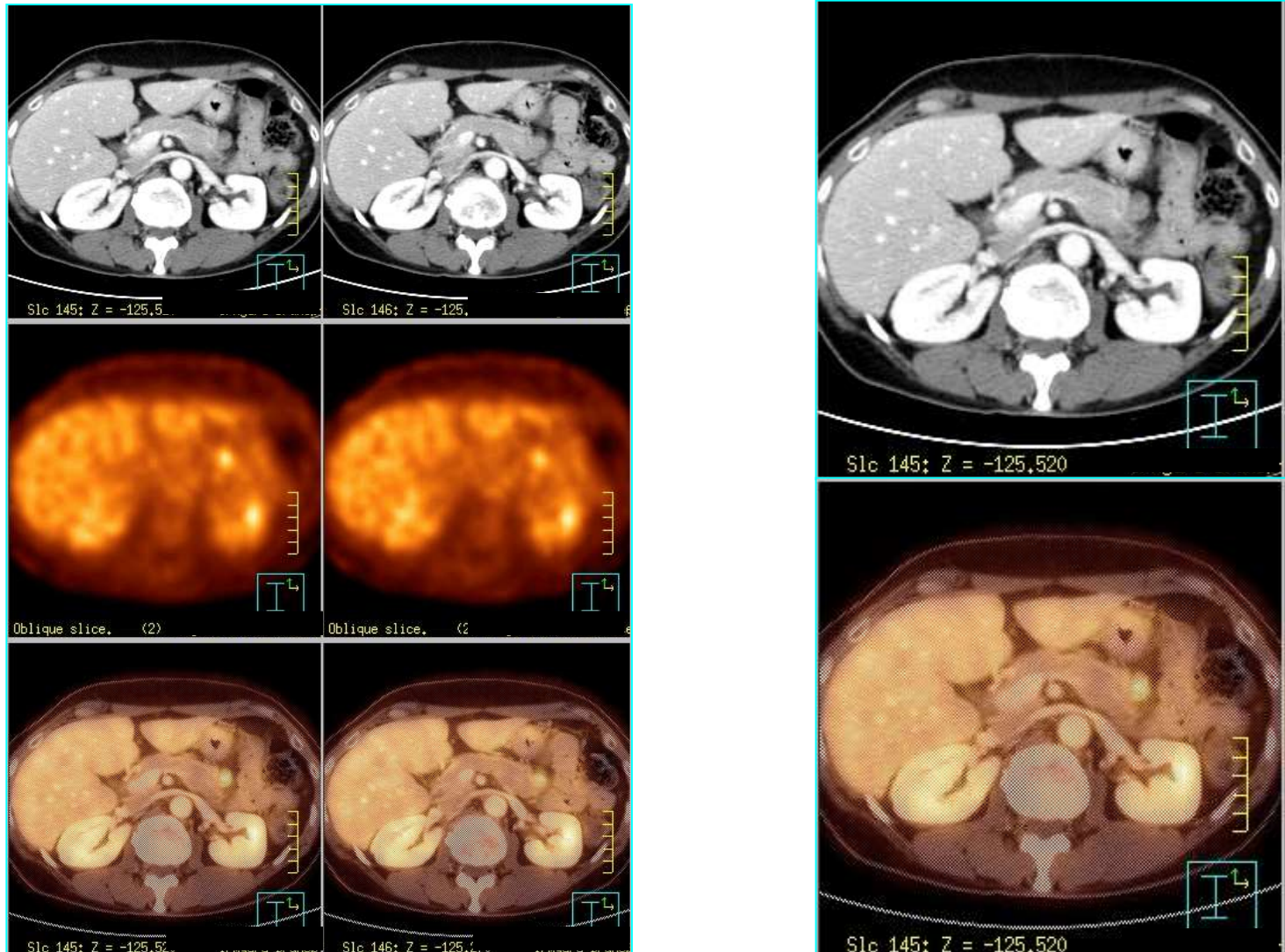
nach 4 Zyklen Chemotherapie (9/04)

- ✓ Primärtumordiagnostik
- ✓ Staging
- ✓ Therapieplanung
- ✓ Therapiemonitoring
- DD Narbe – Rezidiv, Restaging

- 56-jährige Patientin
- Z.n. Entfernung axillärer LK-Metastasen bei Malignem Melanom unbekannter Lokalisation vor 1 Jahr
- Z.n. Entfernung einer Dünndarmmetastase, Restaging





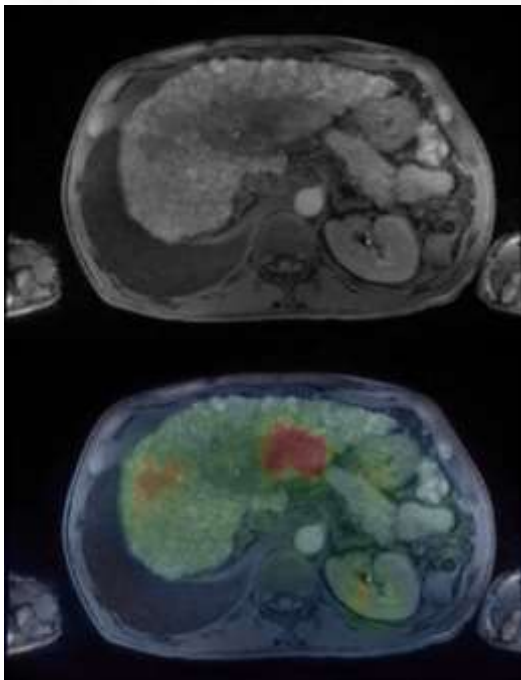
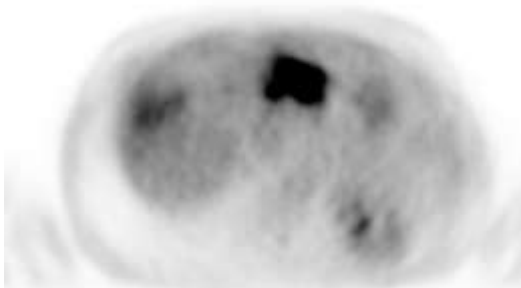


Dünndarmmetastase

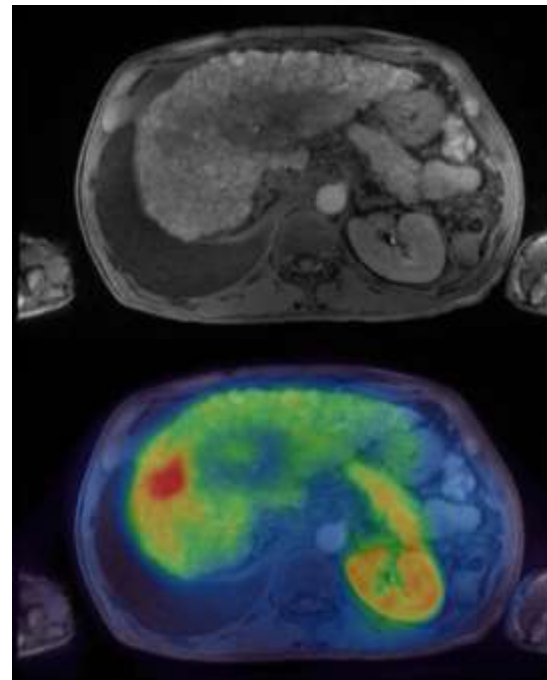
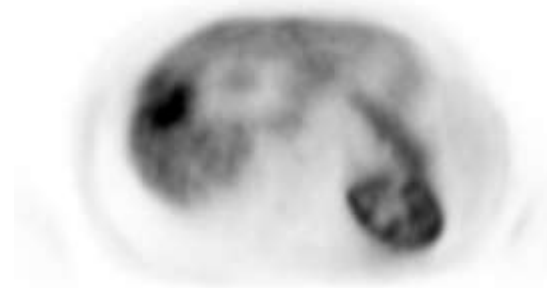
- Geringe Spezifität von FDG
 - DD Entzündung vs. Tumor oft eingeschränkt
 - Dafür: Entzündungs-PET (Vaskulitis, Protheseninfektion)

- Geringe Sensitivität bei verschiedenen onkologischen Entitäten
 - Wenig aggressives Wachstum
 - Hoch differenzierter Tumor: pos. FDG als Zeichen der Entdifferenzierung
 - Hohe „Hintergrund-Aktivität“

^{18}F FDG PET-MR



^{11}C Choline PET-MR

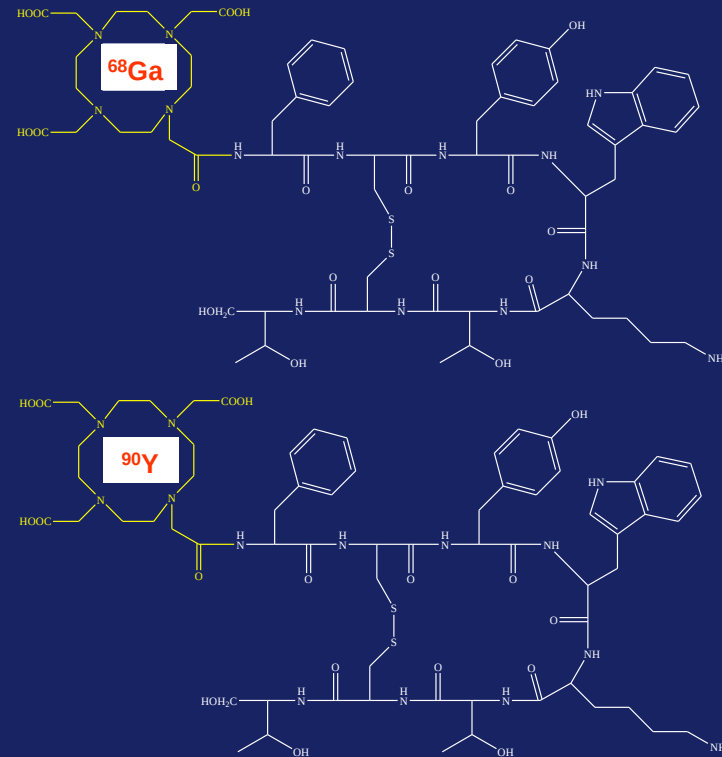


- Glukosemetabolismus:
 - FDG
- Aufnahme/Decarboxylierung von Vorläufern der biogenen Amine Dopamin/Serotonin
 - F-Dopa
- Somatostatinrezeptorbesatz
 - [^{68}Ga]DOTA-TATE
- Lokalisation von gut bis mittelgradig (Proliferationsindex Ki-67 bis 20%) differenzierten NET und deren Metastasen (Tumorsuche/Staging)
- Rezidivdiagnostik bei ansteigenden Tumormarkern und Therapie-monitoring
- Indikationsstellung und Therapie-kontrolle einer Somatostatin-Rezeptor-vermittelten Radiopeptid-therapie

^{68}Ga -DOTATATE

^{90}Y -DOTATATE

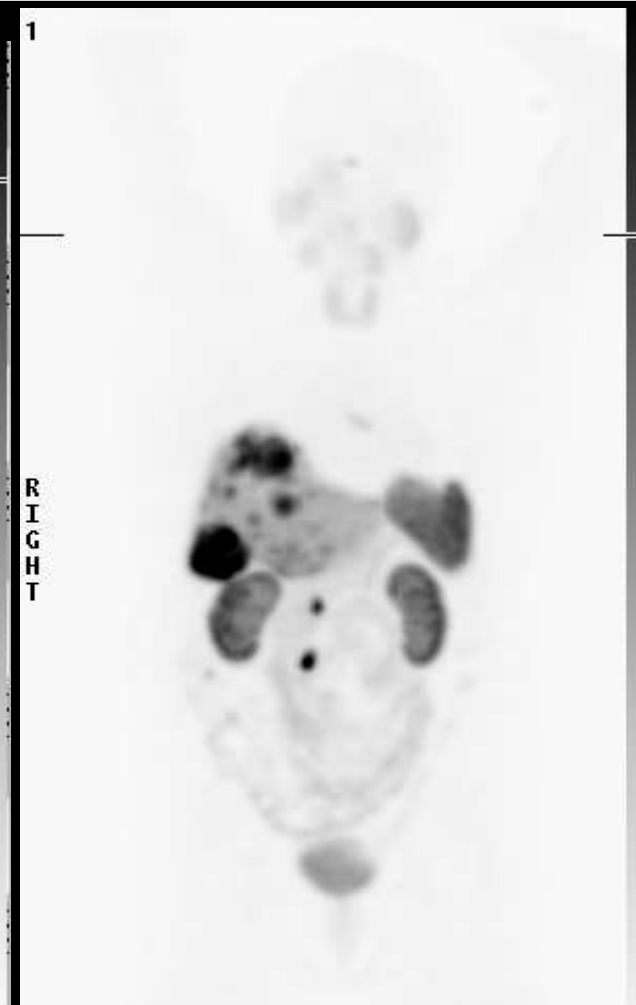
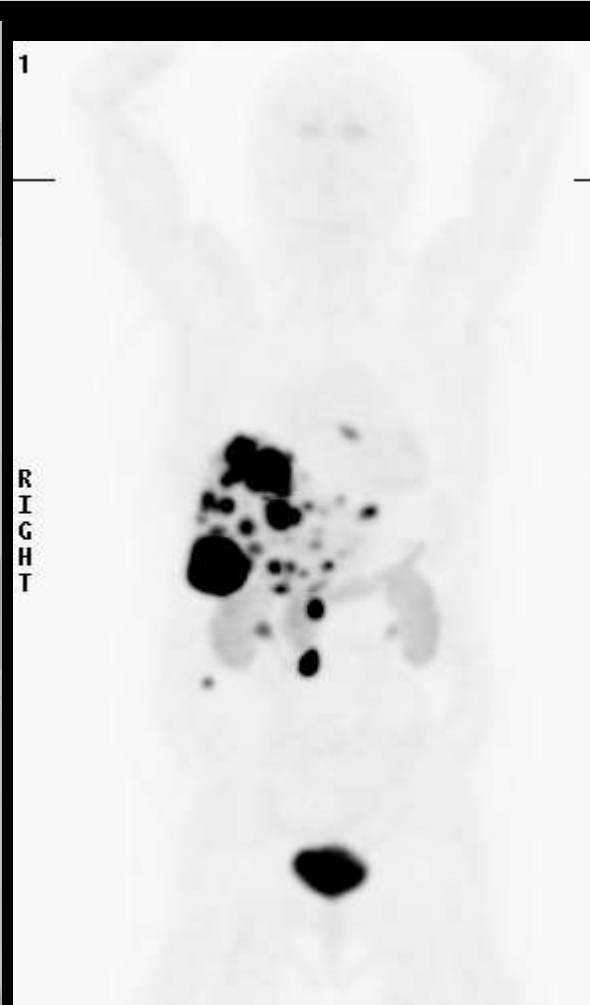
^{177}Lu -DOTATATE



^{18}F -FDG

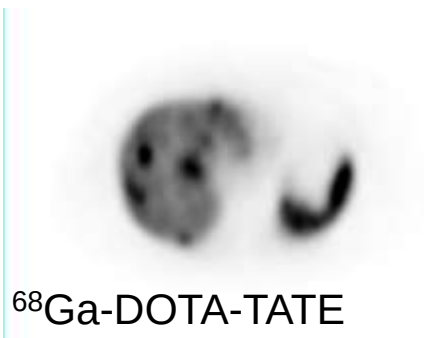
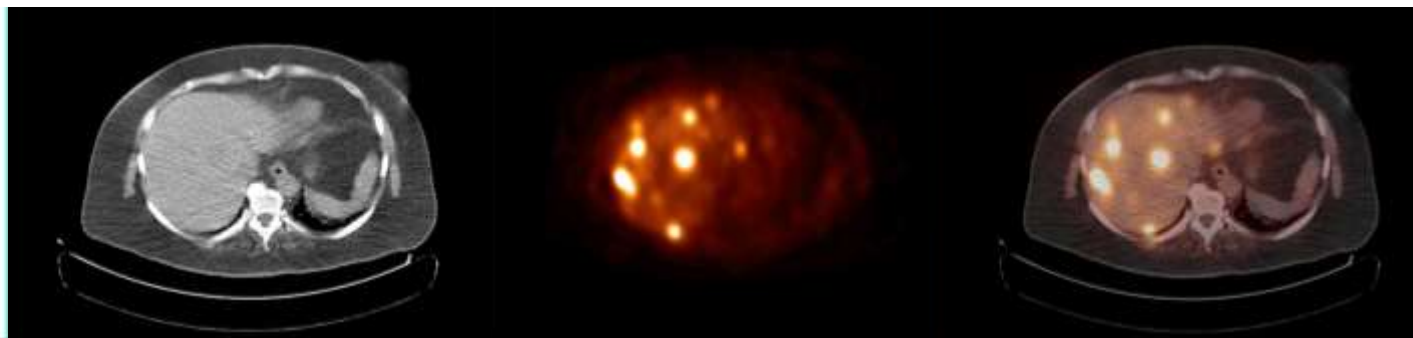
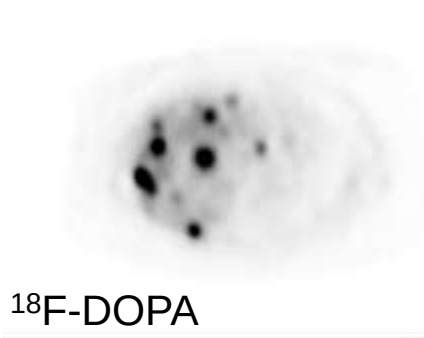
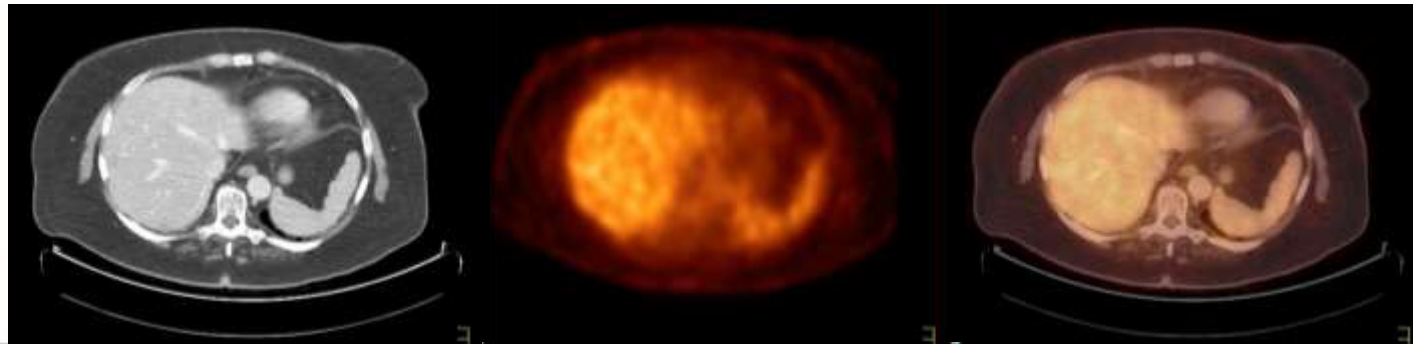
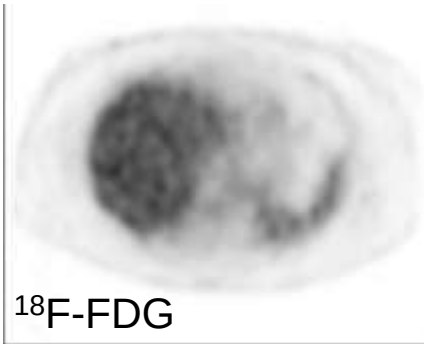
^{18}F -DOPA

^{68}Ga -DOTA-TATE



55 j. Patientin Karzinoid mit Leberfiliae, Prä-SIRT

DOTA-TATE Therapie

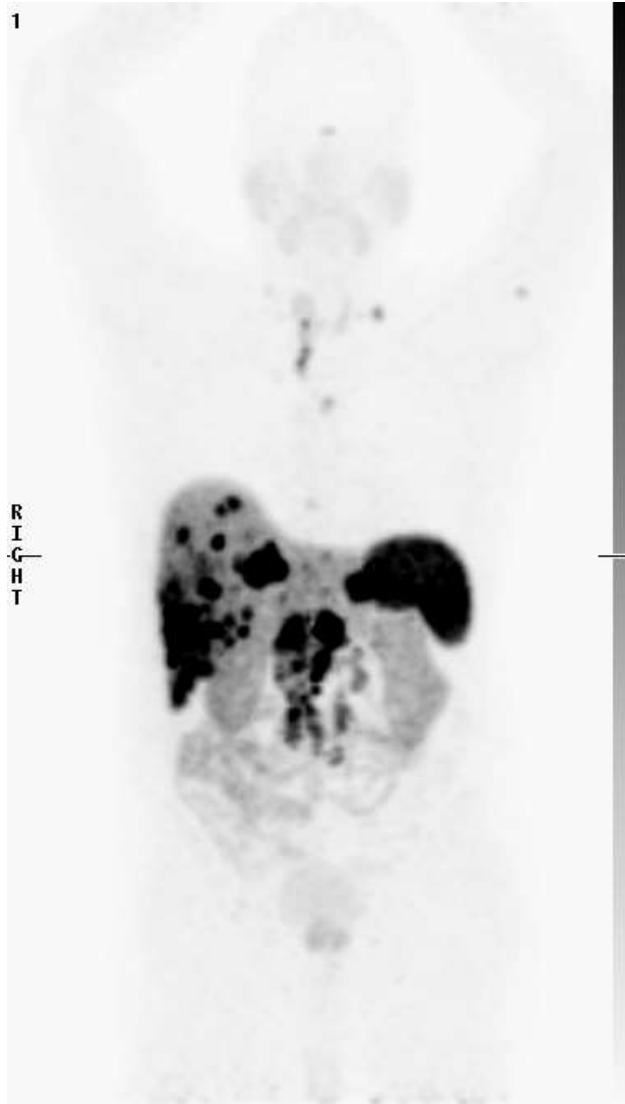


CT (Weichteilfenster)

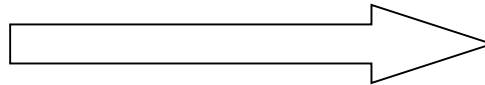
PET

PET/CT (Fusion)

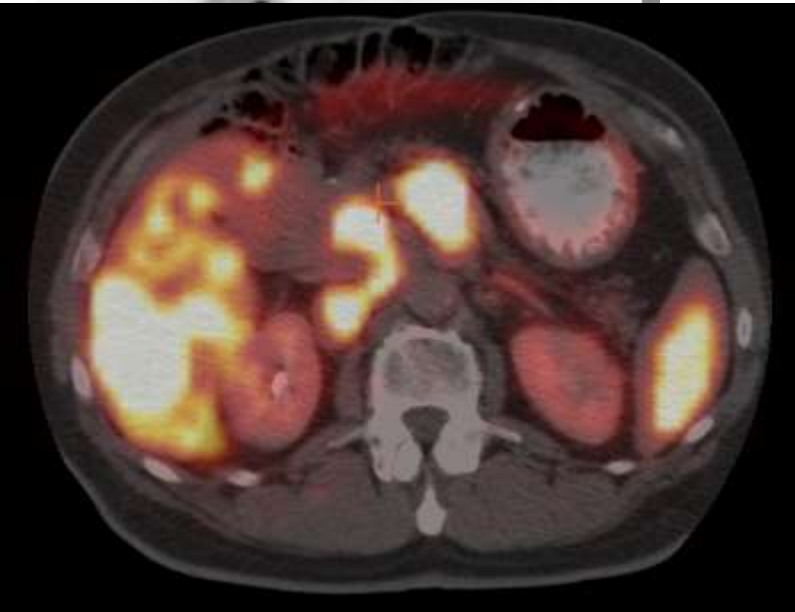
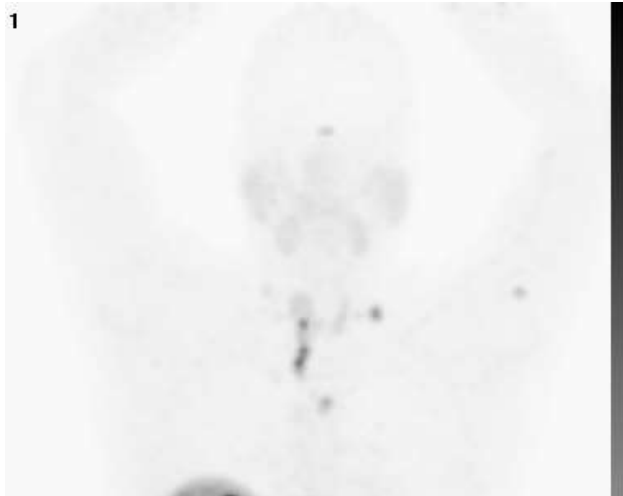
60-jähriger Patient mit NET des Pankreas



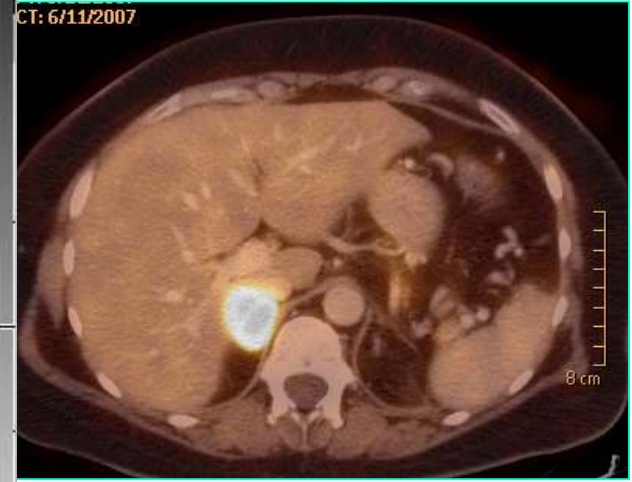
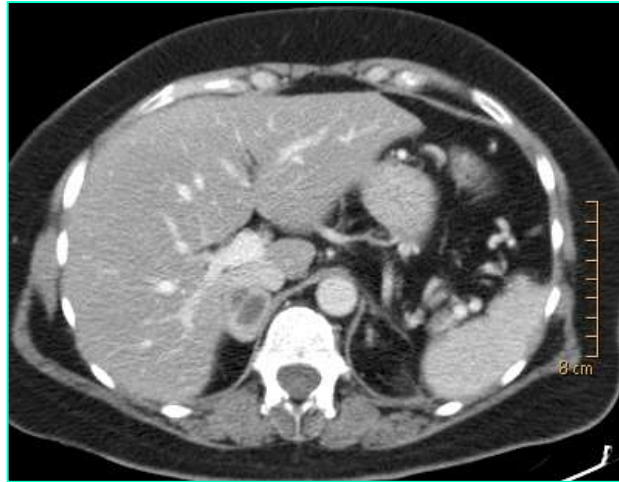
Z.n. 2 x Therapie
mit je 7400 MBq
 ^{177}Lu -DOTATATE



60-jähriger Patient mit NET des Pankreas



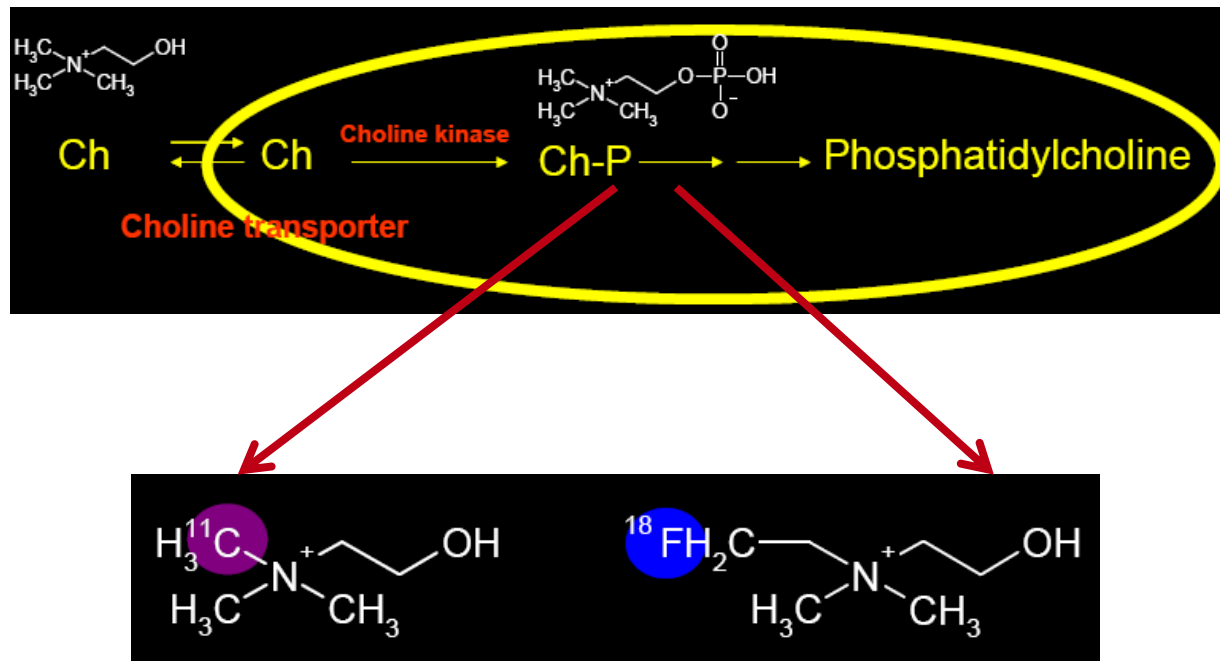
Nebennierentumor (F18-DOPA)



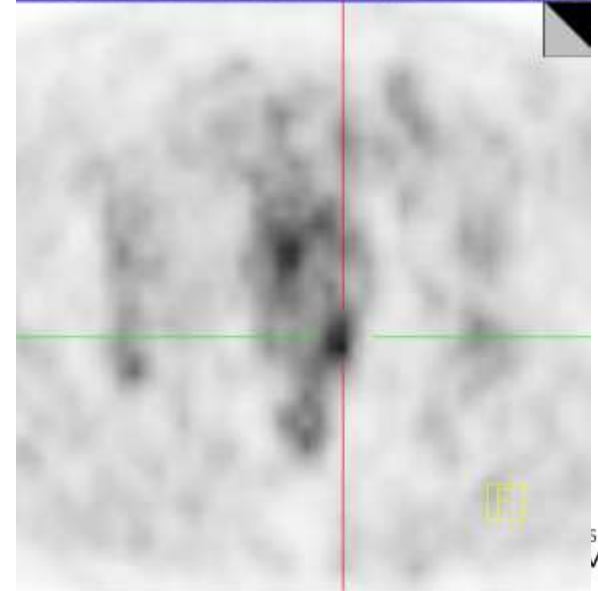
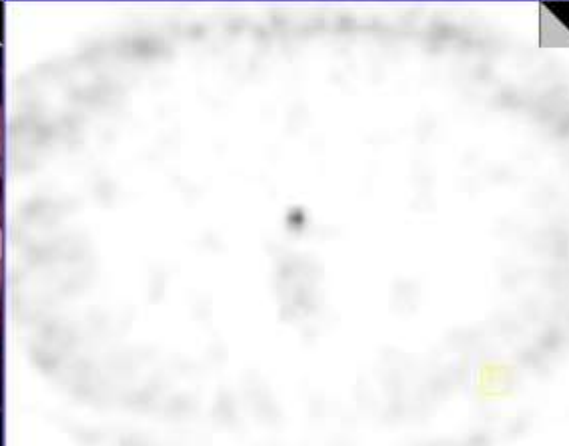
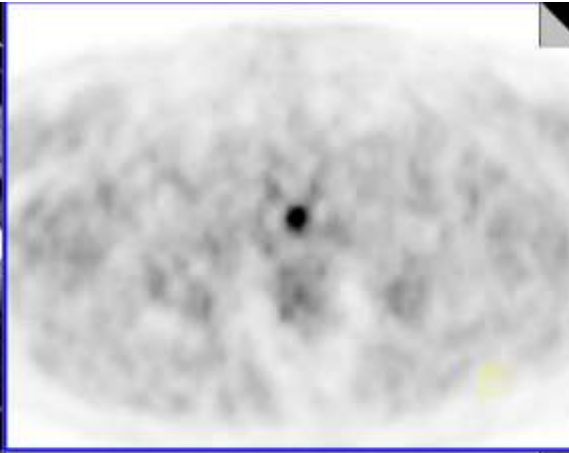
Phäochromozytom: Tumor des Nebennierenmarks

- L-DOPA
 - Aminosäure, an verschiedene Stoffwechselvorgänge beteiligt
 - Vorläufer verschiedener biologisch relevanter Stoffe (u.a. Melanin, Dopamin, Adrenalin und Noradrenalin)
- F18-DOPA wird verwendet in der Diagnostik :
 - **neuroendokriner Tumore** (z.B. Phäochromozytome, Paragangliome)
 - medulläres **Schilddrüsenkarzinom**

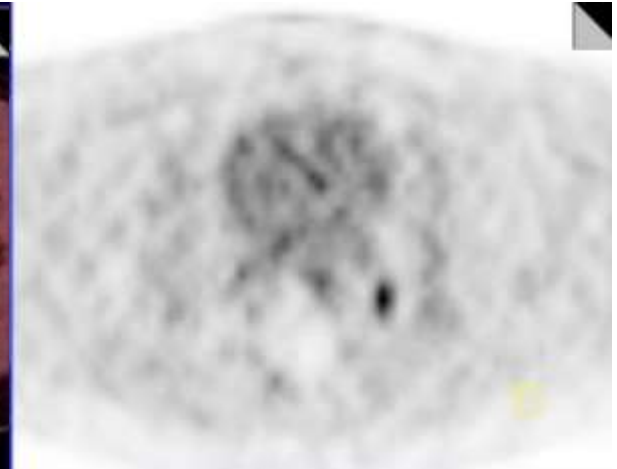
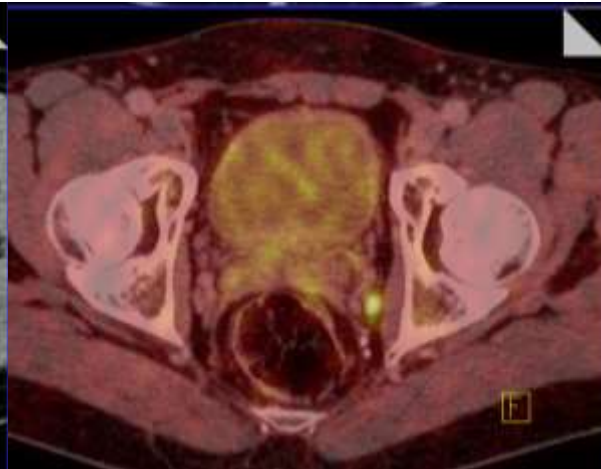
- Prostata-Ca sind meistens FDG-negativ
 - Ausnahme: wenige entdifferenzierte, aggressiv wachsende
 - FDG bei Prostata-Ca nicht indiziert!!
- Cholin:
 - natürliche Aminosäure: wichtiger Bestandteil der Zellmembran



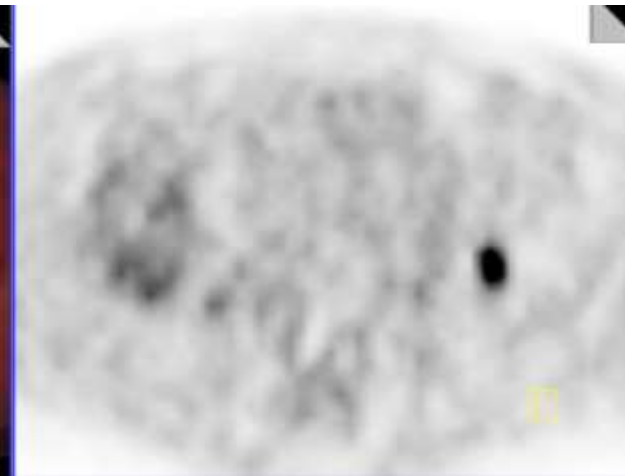
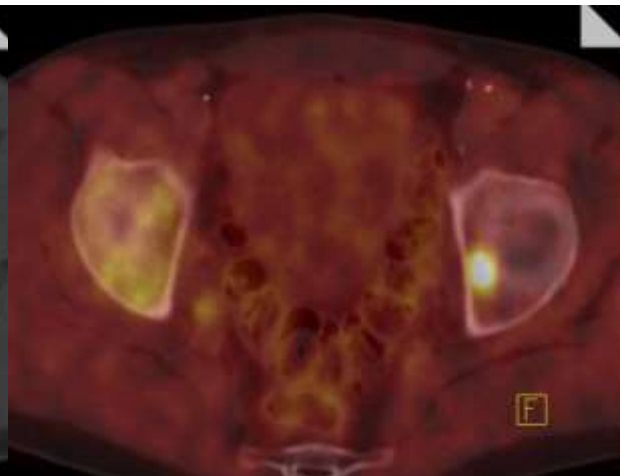
local status



nodal status



bone status



- Cholin-Aufnahme ist jedoch abhängig von PSA

➔ **PSA 1-2 ng/ml $\approx$ DR: 40 - 50%**

➔ **PSAdt: > 6m = DR 27%**
< 6m = DR 61%
< 3m = DR 81%

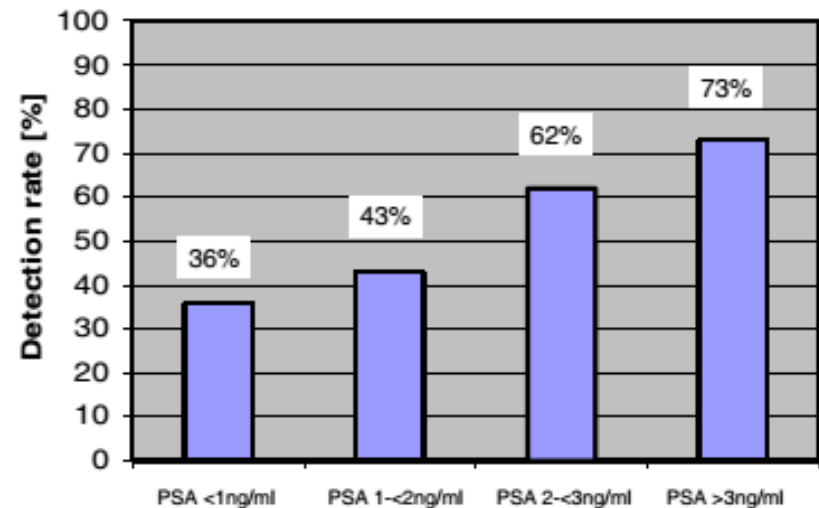
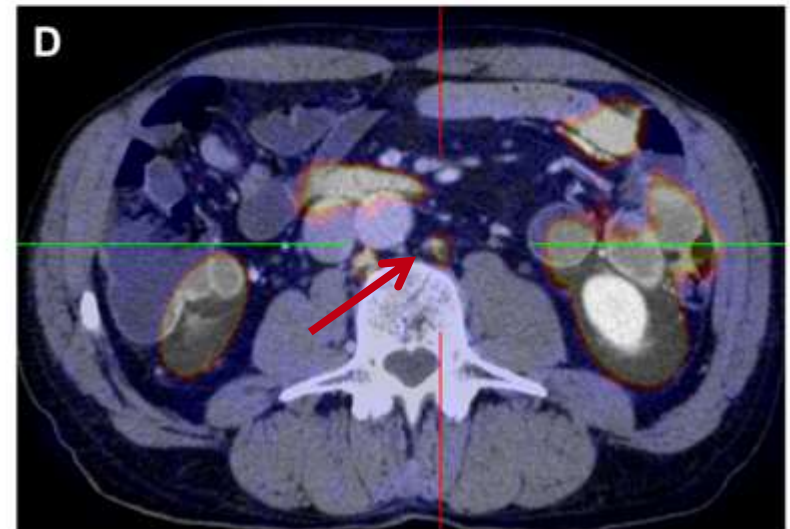
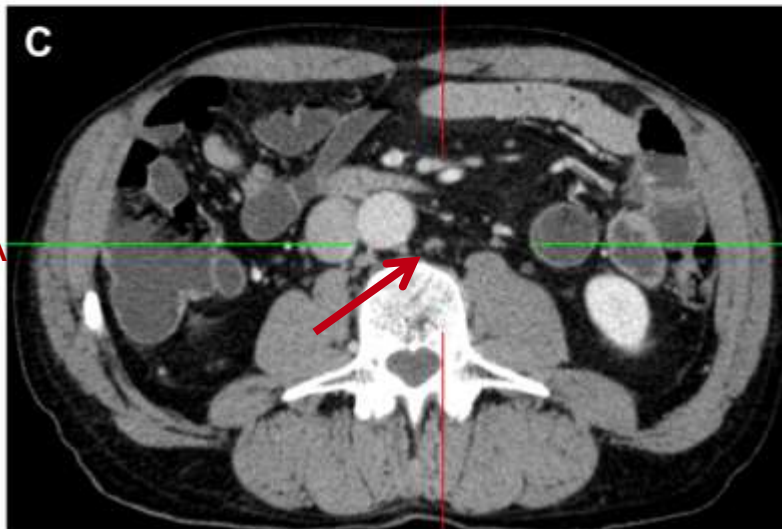
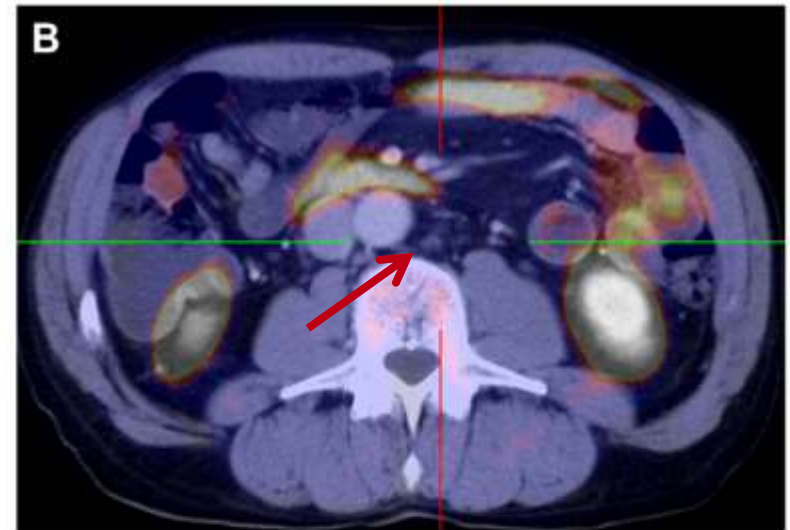
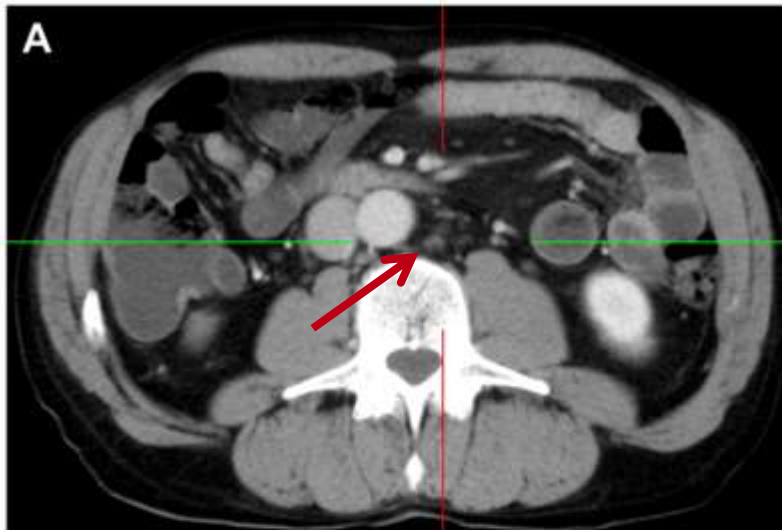


Fig. 1 Detection rate of [^{11}C]Choline-PET/CT plotted against the PSA-value for recurrent prostate cancer

- Suche nach verbesserten Radiopharmaka!**



- Höhere Detektionsrate durch neue Radiopharmaka!

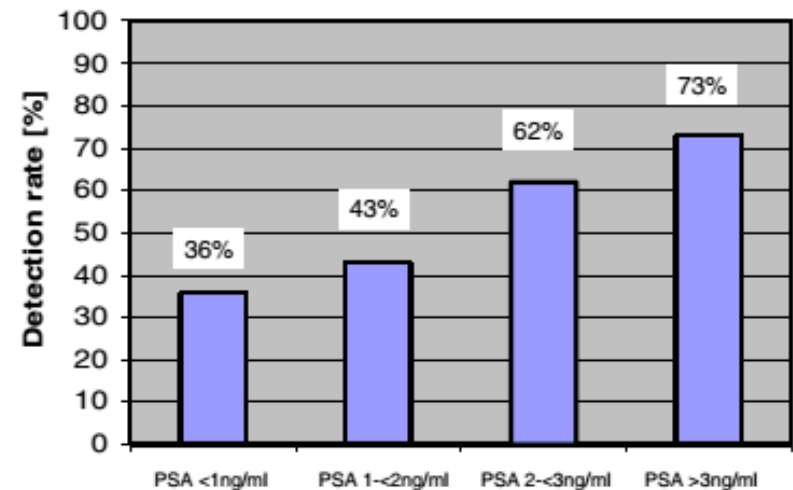
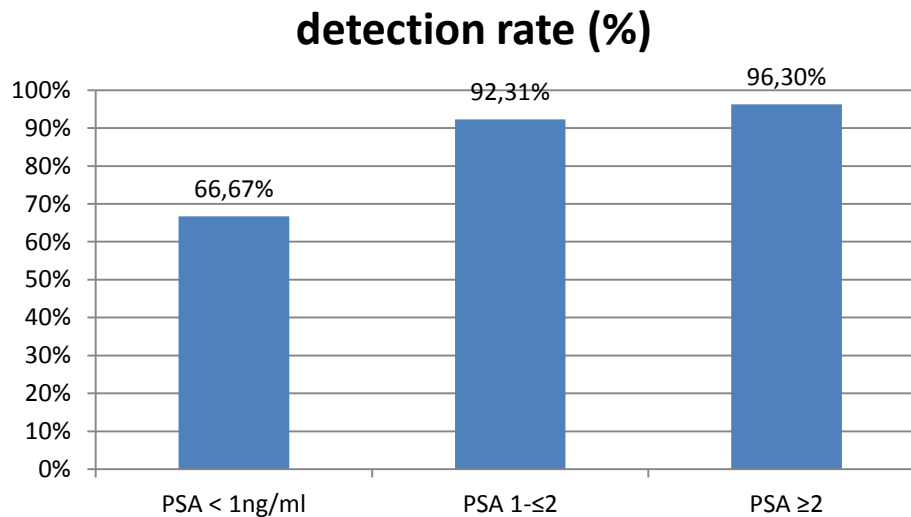


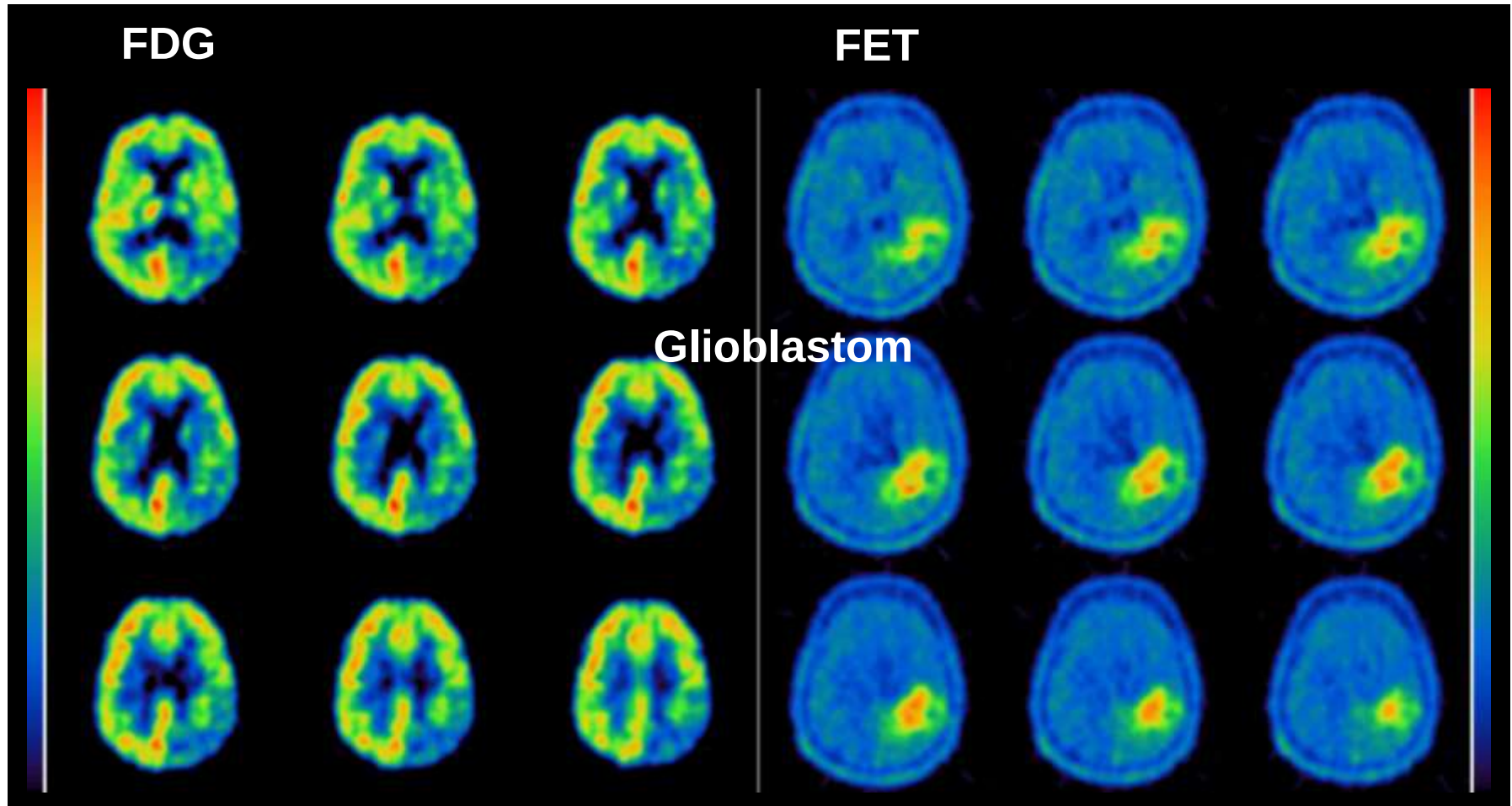
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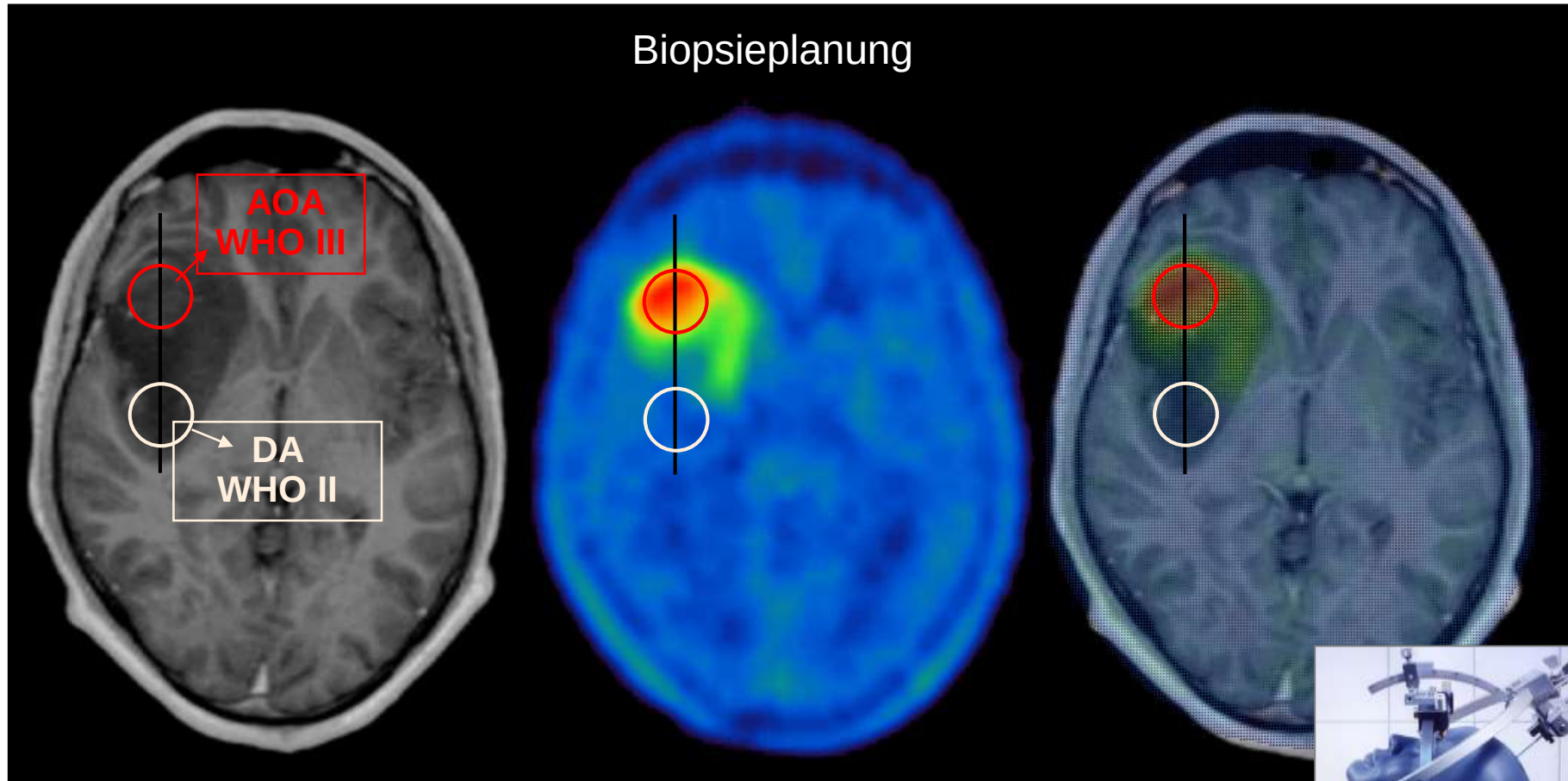
- Hirntumoren
- Demenz
- Epilepsie
- Parkinson Syndrome

- 50% (bis 90%) aller hirneigener Tumoren; Inzidenz: $\sim 10 / 10^5/y$

	WHO Grade	Nomenclature	Histology / Mol. Diagnostic
low grade (LGG)	I	Pilocytic Astrocytoma	Piloid cells, biphasic growth pattern
	II	Astrocytoma <i>Oligodendroglioma</i> <i>Oligoastrocytoma</i>	cellular atypia <i>Oligo: LOH 1p/19q</i>
high grade (HGG)	III	Anaplastic Astrocytoma <i>Anaplastic Oligoastrocytoma</i> <i>Anaplastic Oligodendroglioma</i>	high cell density, mitotic activity increased cellular atypia, <i>Oligo: LOH 1p/19q</i>
	IV	Glioblastoma	necrosis, high cellular polymorphism, endothelial proliferation

- 5-J Überleben:
 - LGG 70% (pilocytic Astrocytoma or Oligodendroglioma)
 - GBM 3 - 4%

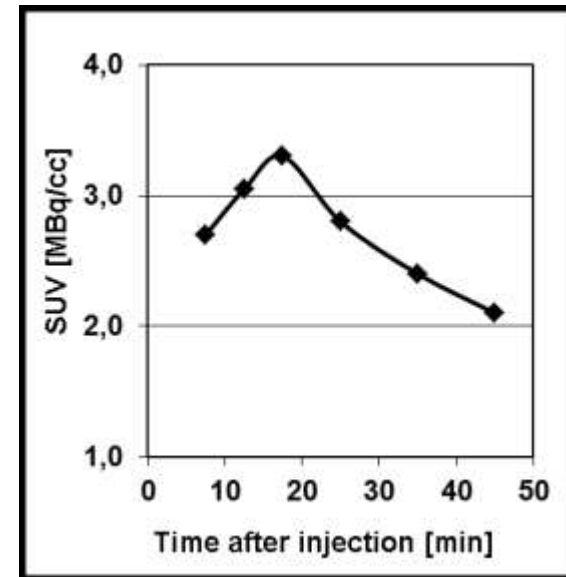
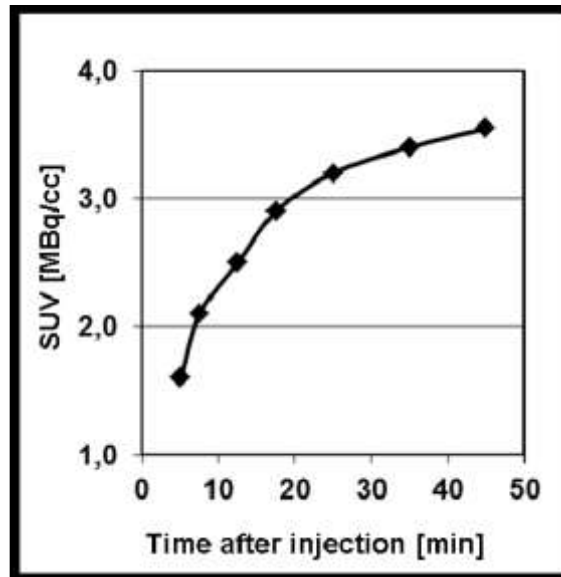




- amino acid uptake only partially correlates with histological grade
 - trend to higher uptake in HGG
 - higher uptake in Oligo-tumors (*Jansen et al. NeuroOncol 2012*)
- conventional amino acid uptake does not allow grading on individual level:
 MET (*Ceyssens et al. AJNR 2006*); FET (*Pöpperl et al. EJNMMI 2007*); F-DOPA (*Fueger et al. JNM 2010*)
- dynamic analysis of FET-uptake is discussed controversially
 for the differentiation between LGG vs. HGG (*Pöpperl et al. EJNMMI 2007*,
Kunz et al. NeuroOncol 2011, *Jansen et al. EJNMMI 2012*)

LGG: increasing TACs

HGG: decreasing TACs

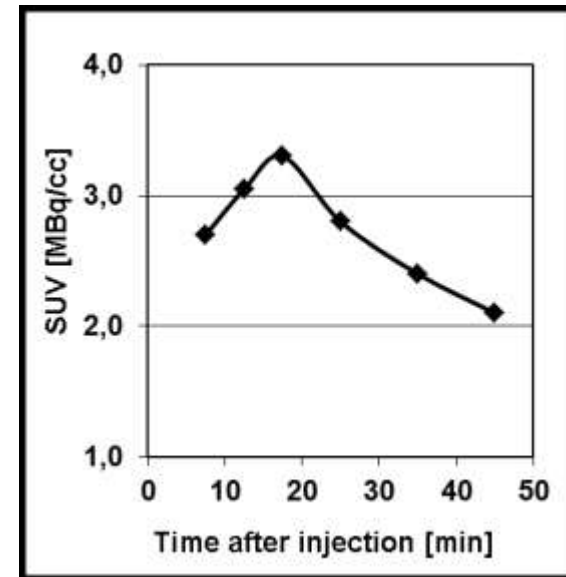
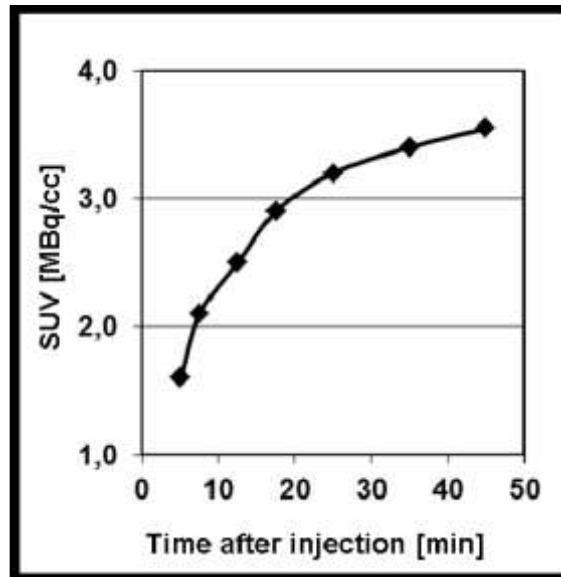


- amino acid uptake only partially correlates with histological grade
 - trend to higher uptake in HGG
 - higher uptake in Oligo-tumors (*Jansen et al. NeuroOncol 2012*)
- conventional amino acid uptake does not allow grading on individual level:
 MET (*Ceyssens et al. AJNR 2006*); FET (*Pöpperl et al. EJNMMI 2007*); F-DOPA (*Fueger et al. JNM 2010*)
- dynamic analysis of FET-uptake is discussed controversially
 for the differentiation between LGG vs. HGG (*Pöpperl et al. EJNMMI 2007*,
Kunz et al. NeuroOncol 2011, *Jansen et al. EJNMMI 2012*)

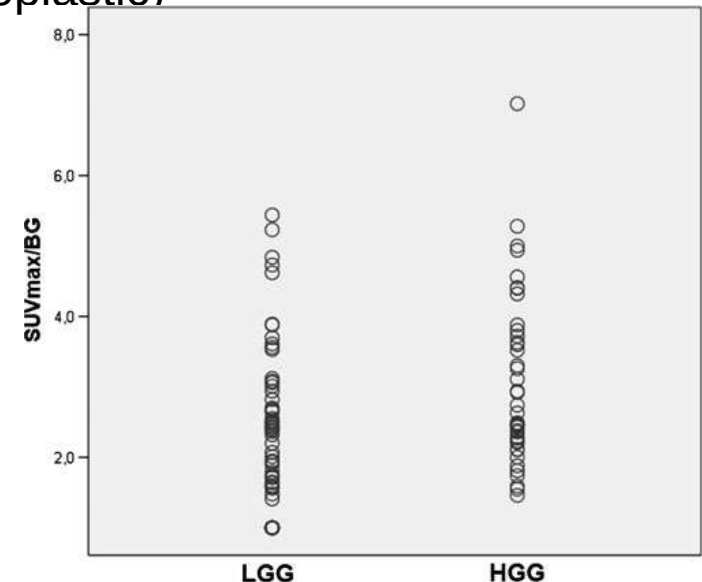
➔ LGG: increasing TACs

HGG: decreasing TACs

➔ independently from
FET-uptake



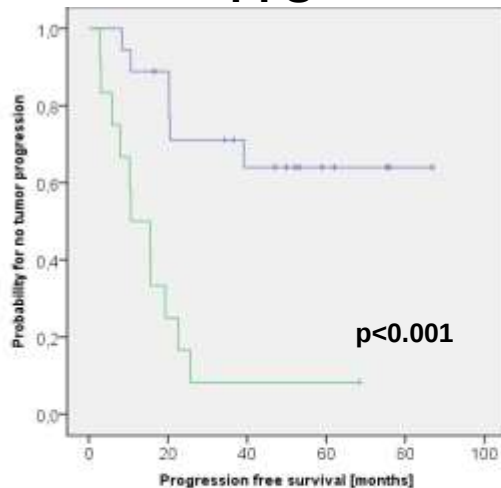
- 127 patients with newly diagnosed MRI-suspected LGG
 - histopathology: 71 LGG, 47 HGG (including 5 GBM)
- Findings:
 - reduced uptake: 11 cases (7 LGG & 4 HGG)
 - normal tracer uptake: 19 cases (15 LGG, 1 HGG & 3 non-neoplastic)
 - increased uptake: 97/127 patients (4 non-neoplastic)
 - no differentiation between HGG & LGG with conventional uptake parameters



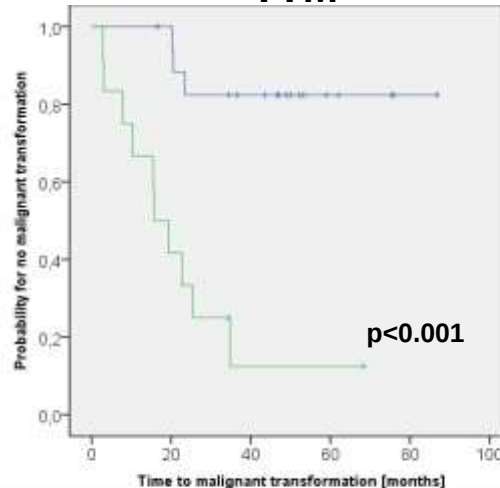


FET-positive astrozytische Low Grade Gliome mit abfallender Kinetik haben einen schlechten Krankheitsverlauf

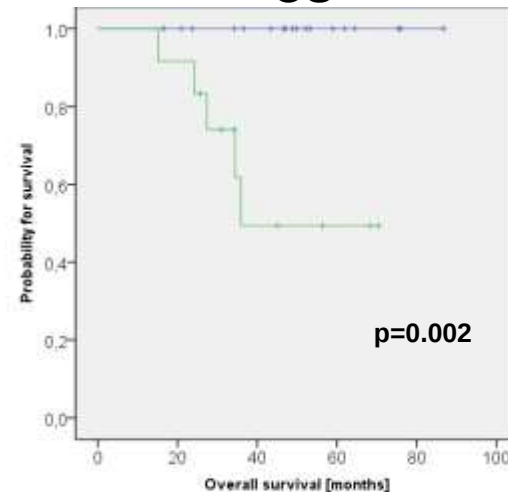
PFS



TTM



OS



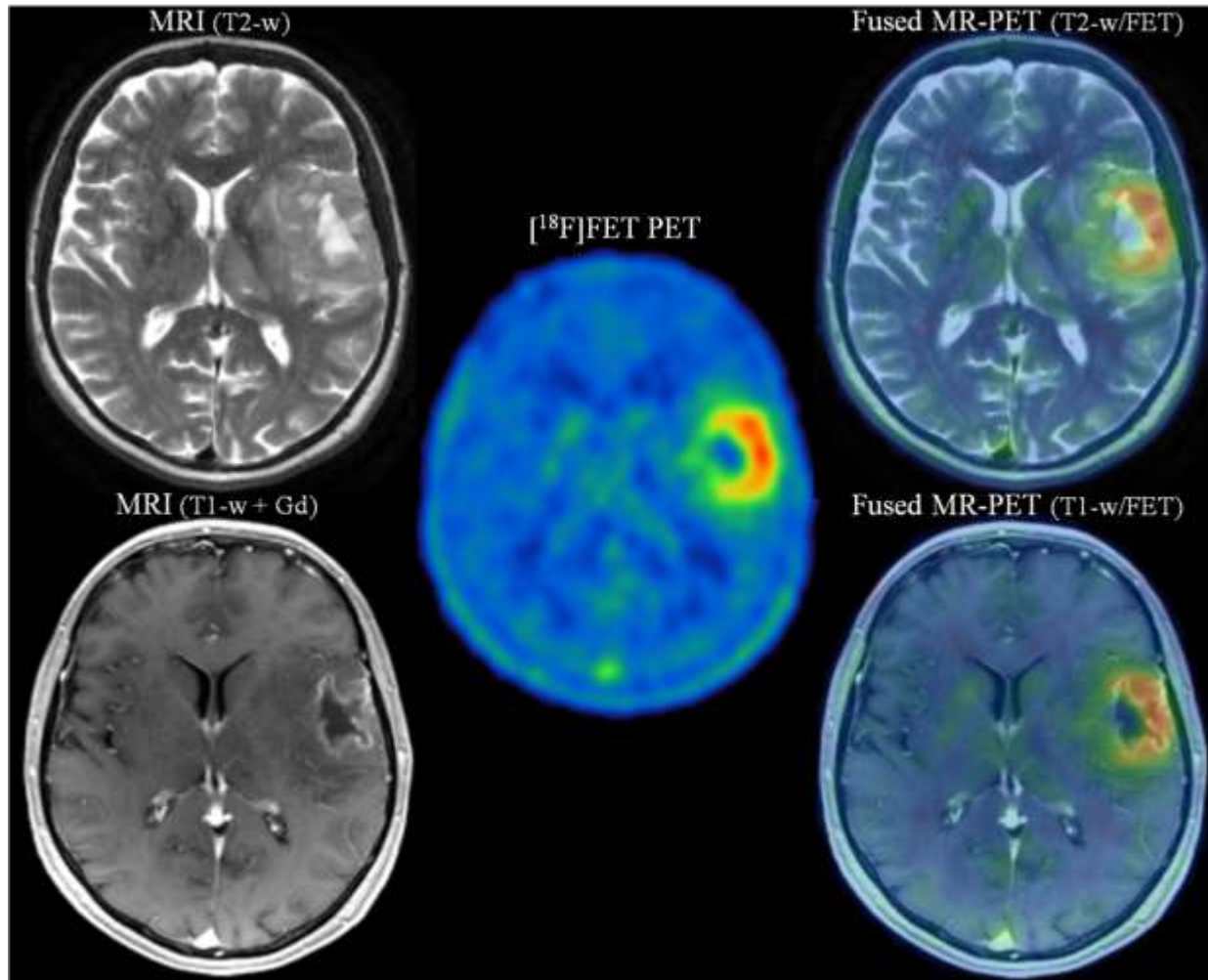
Time-activity-curves

- increasing
- decreasing
- + increasing-censored
- + decreasing-censored



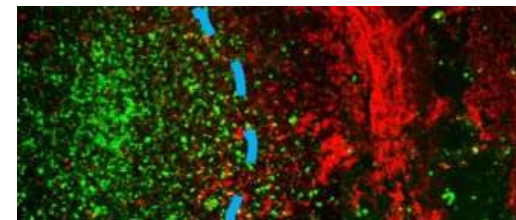
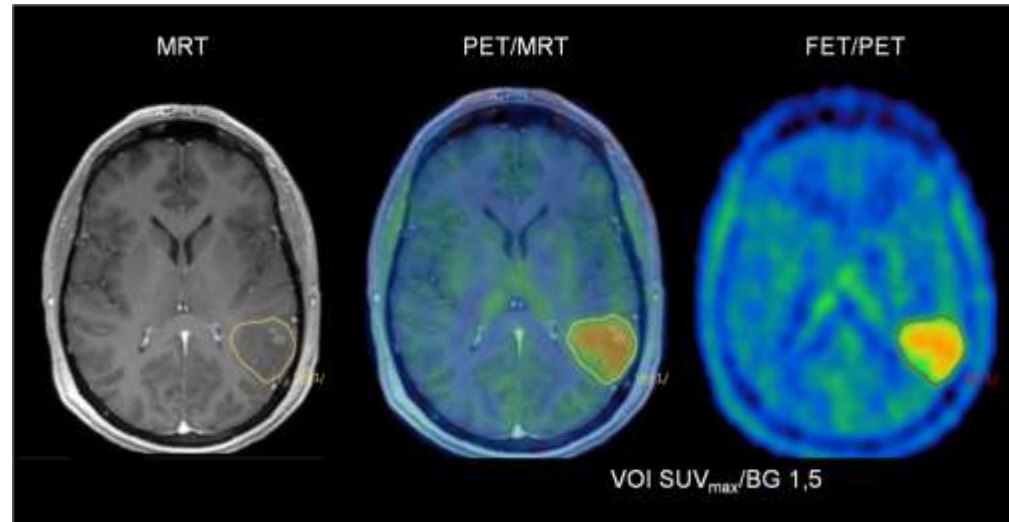
Veränderung der Therapiestratifizierung?

Problematik: Exakte Delineation von vitalem Tumorgewebe / - grenze

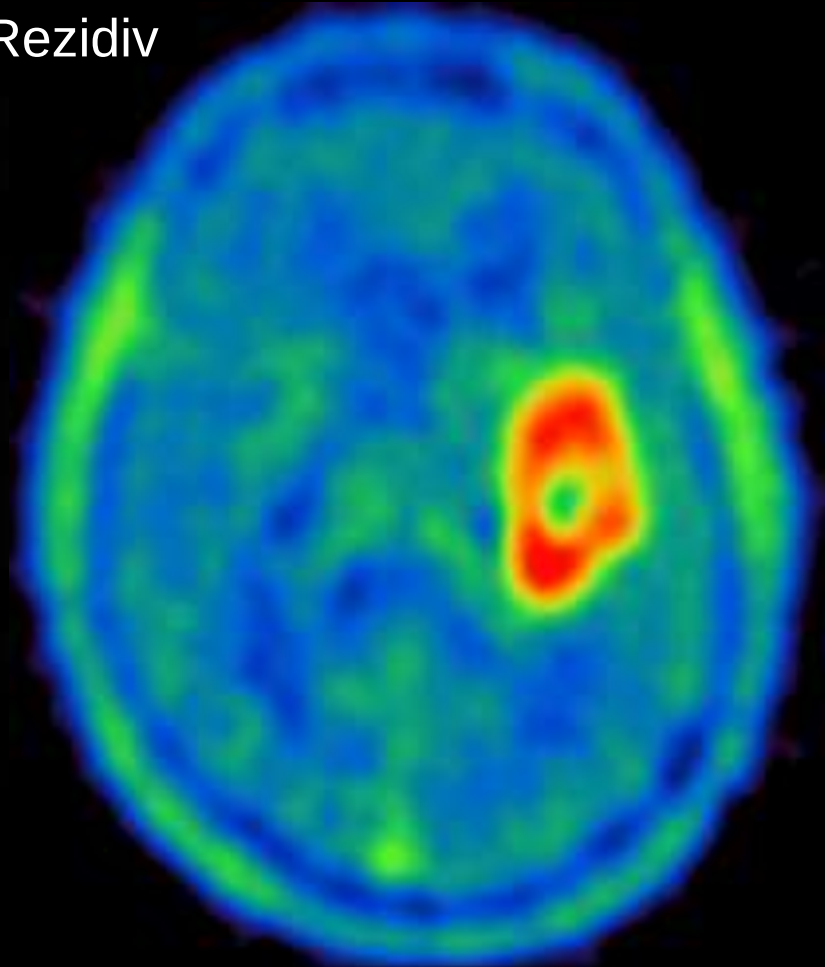


- Therapieplanung-Optimierung?
 - Gewebeschonung
 - Toxizitätsreduktion
 - Höhere Planungssicherheit

- Dosis-Eskalation?
 - 80% Frührezidive im Randbereich des Primärius (2-3 cm)
 - kontinuierliches infiltratives Wachstum
 - unzureichende Zielvolumenbestimmung? (CT & MRT-basiert)

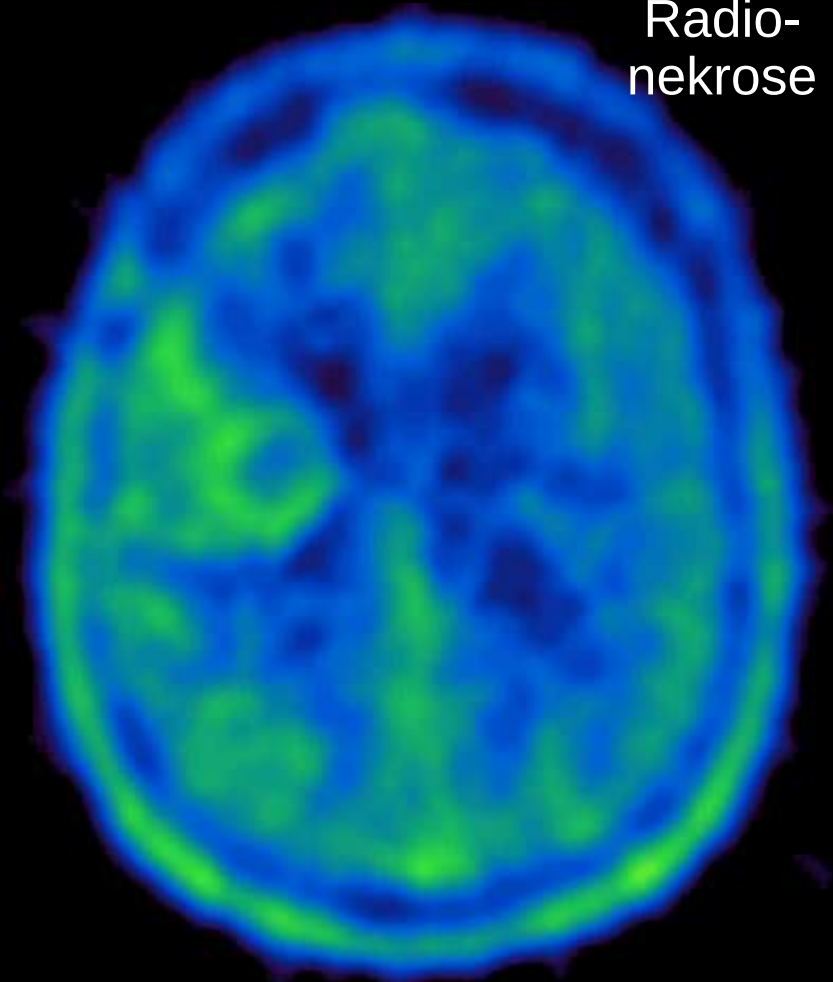


Rezidiv



SUVmax/BG: 5,8

Radio-
nekrose



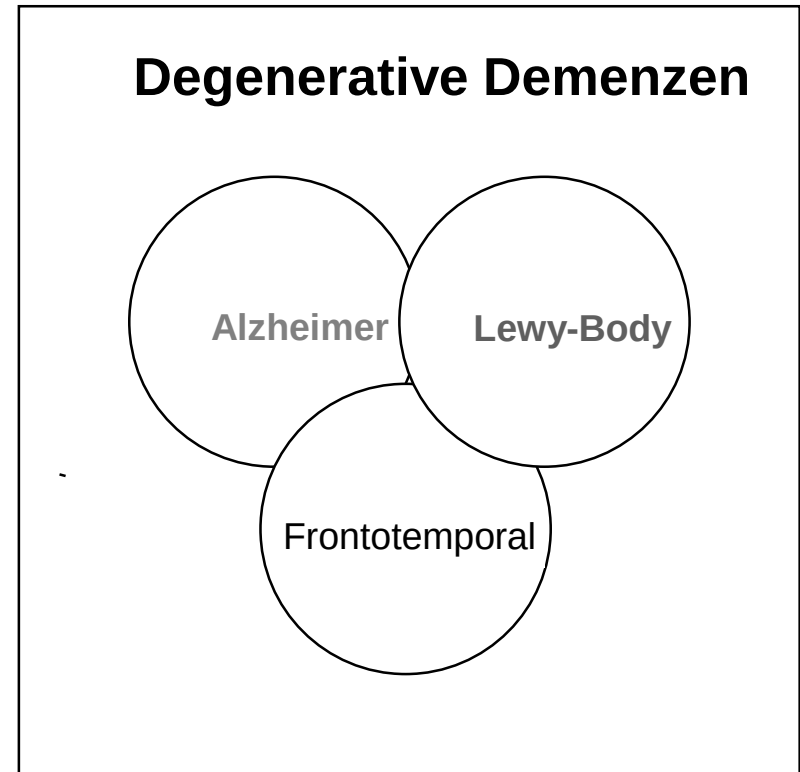
1,7

- ✓ Hirntumoren
- Demenz
- Epilepsie
- Parkinson Syndrome

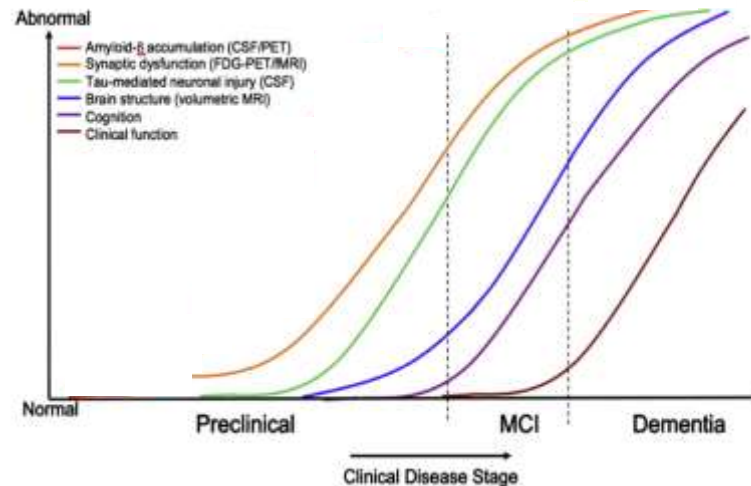
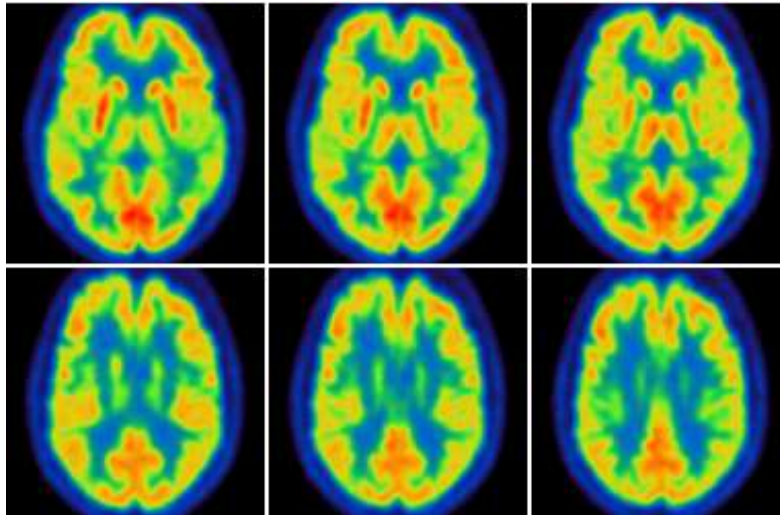
- Neurodegenerativ
 - Alzheimer Typ (DAT) 60-70%
 - Mischform DAT / vaskulär 4-10%
 - Lewy-Body Demenz 5-10%
 - Frontotemporale Lobärdeg. 4%
 - Andere (CJD, HD, CBD, PSP)

- Vaskulär
 - SAE, Infarkt 10-15%

- Andere
 - Trauma, Tumor, Infektion, entzündlich, metabolisch

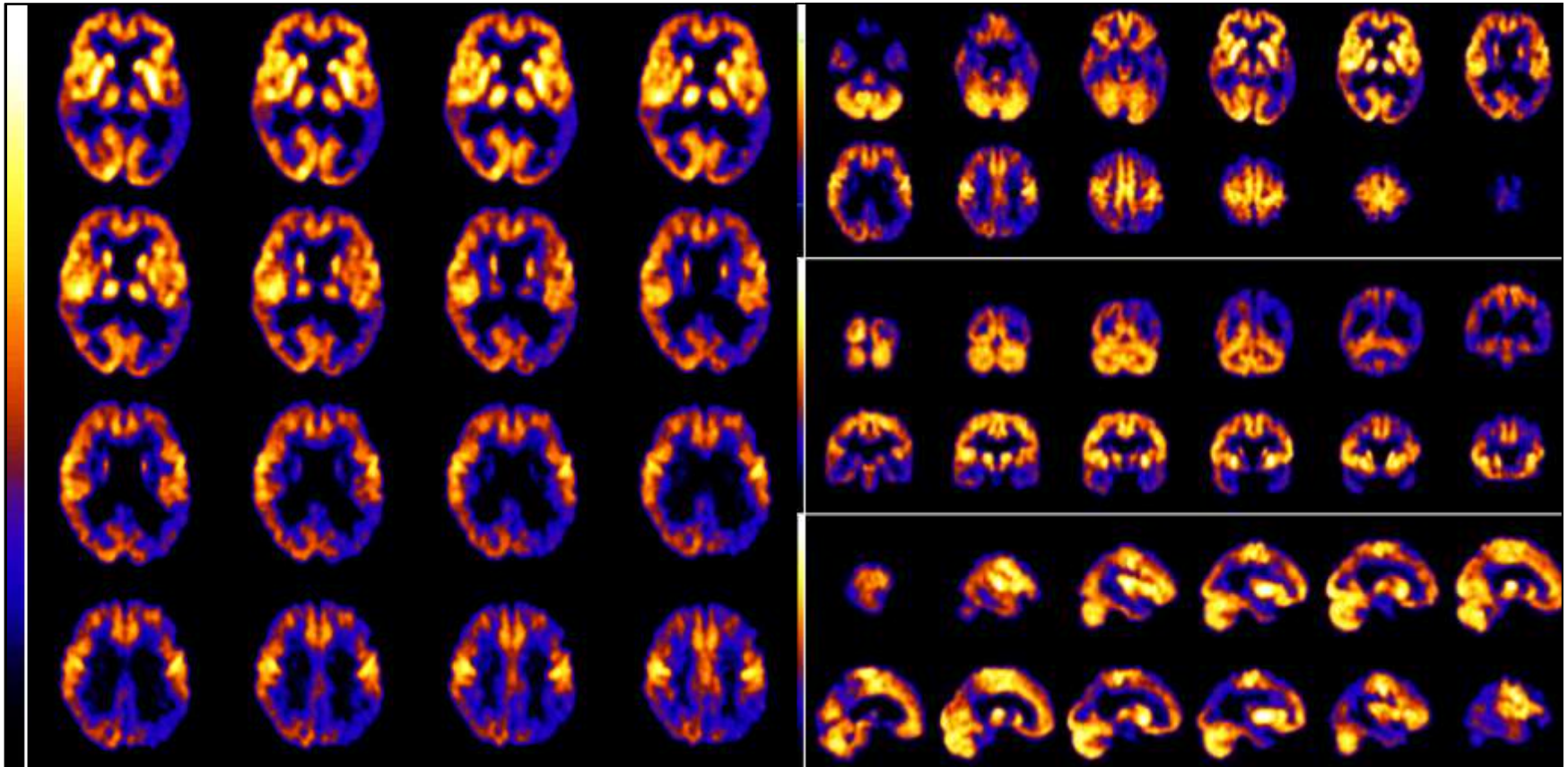


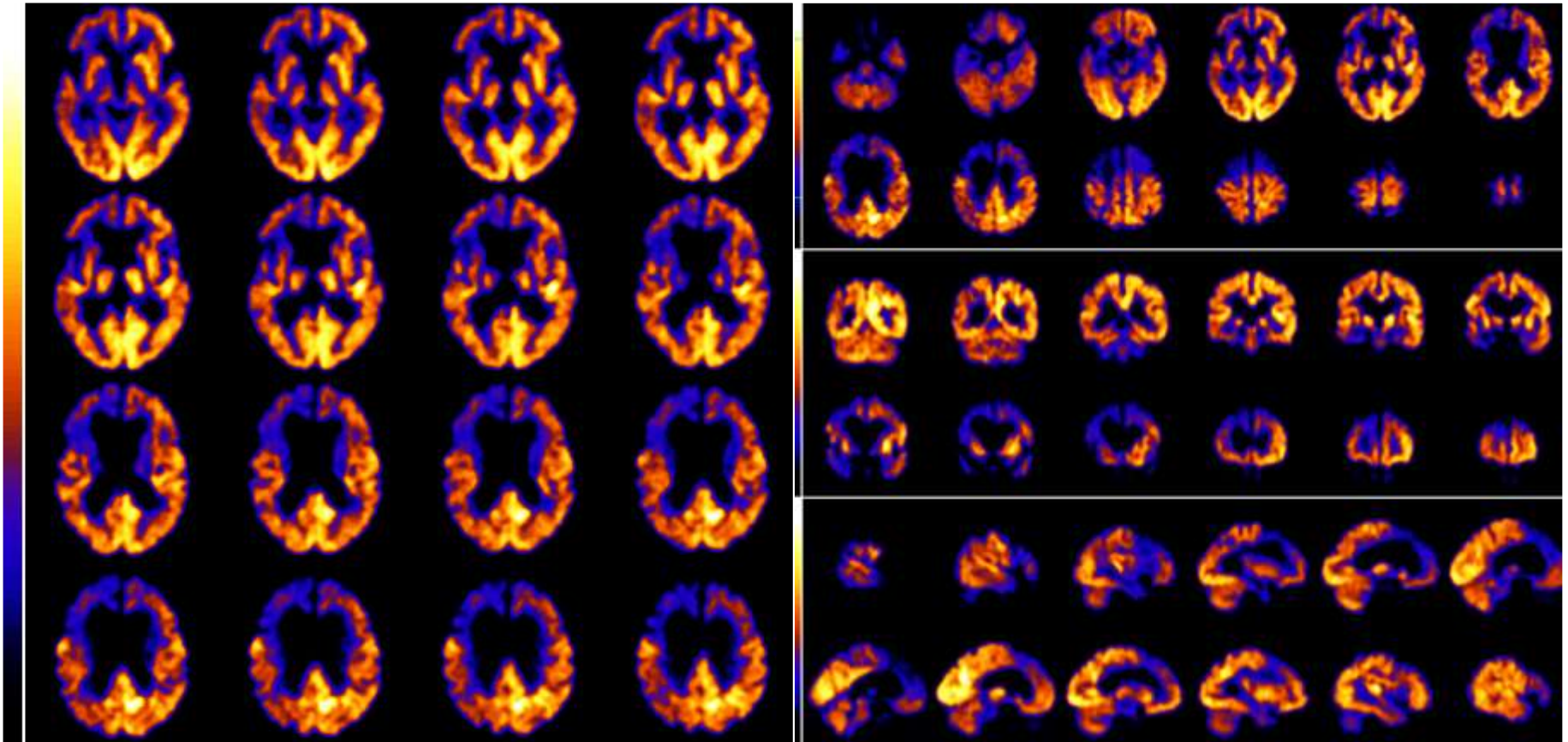
Frühsymptomatisch
(^{18}F FDG)

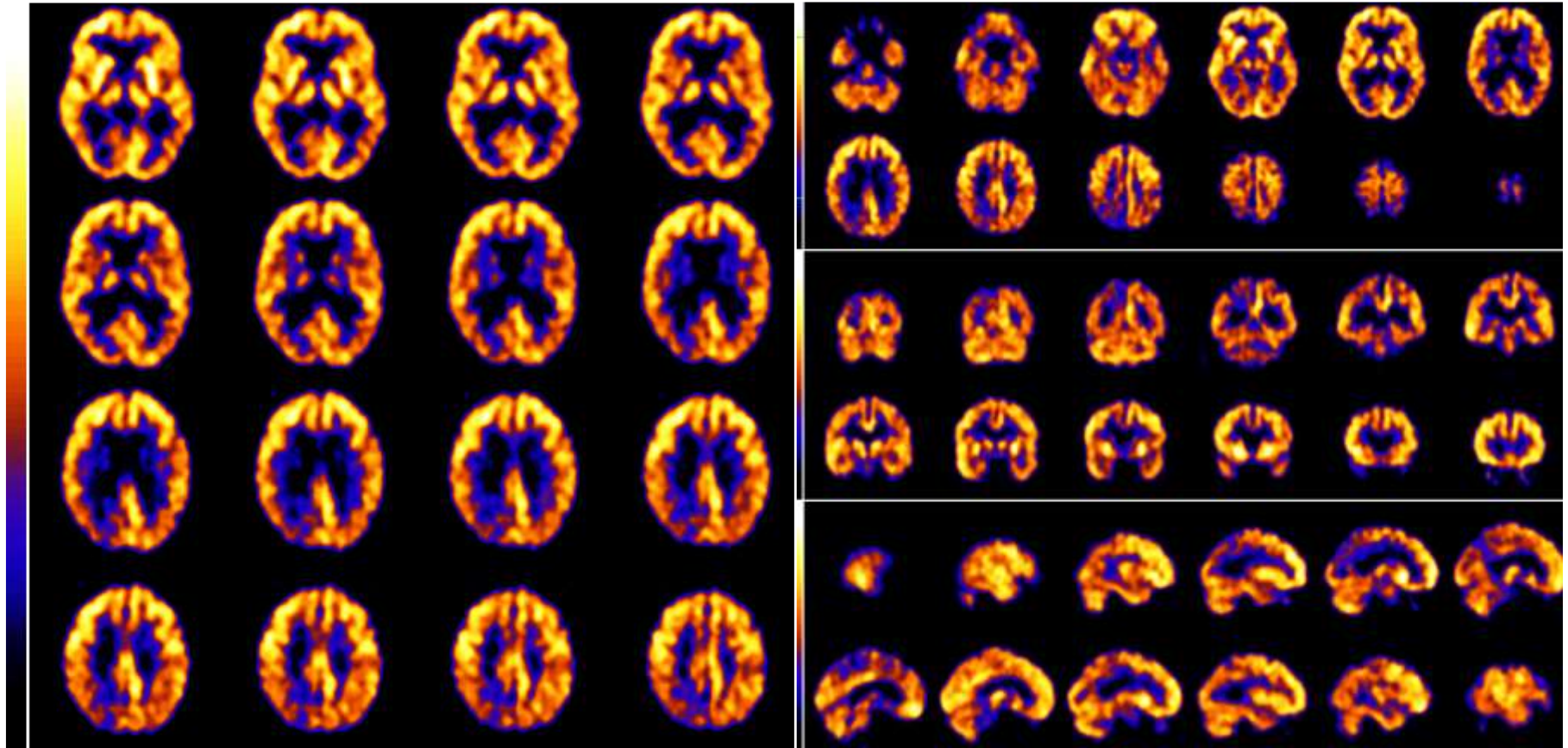


Sperling RA *Alzheimers Dement.* 2011; 7:280-92

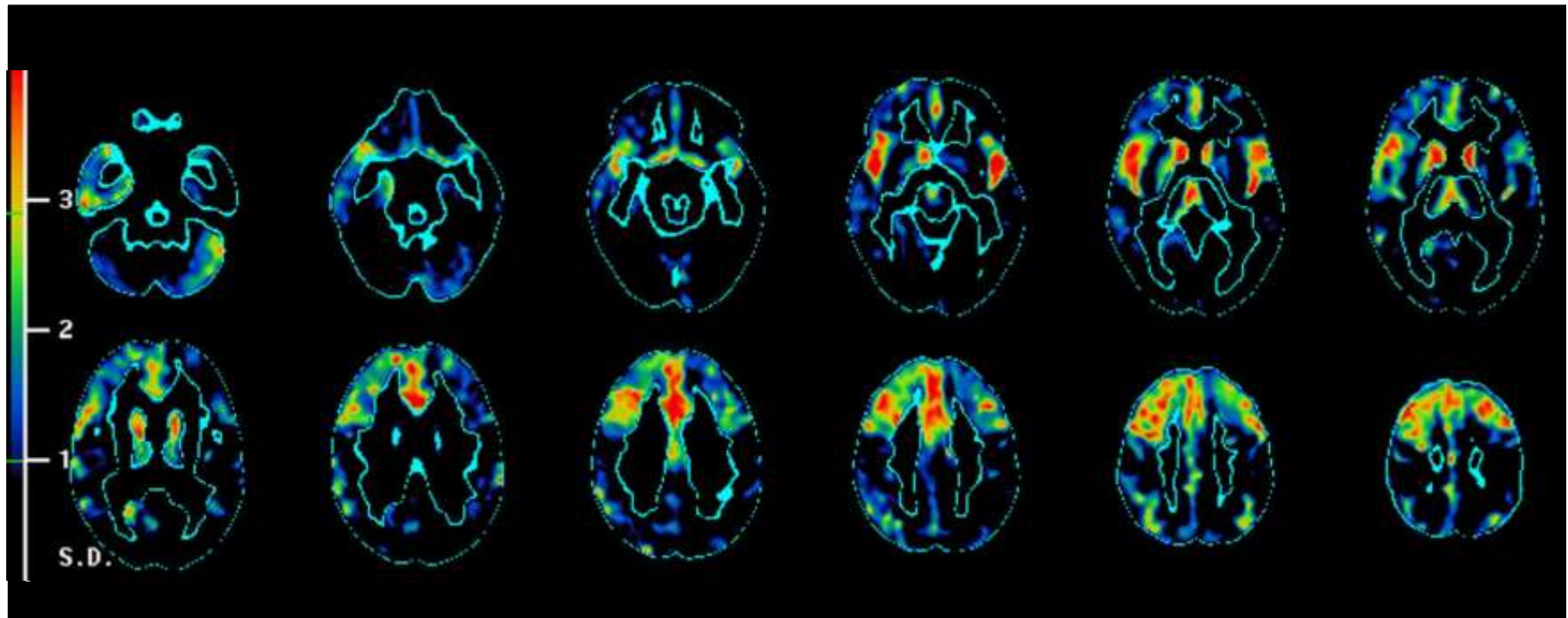
Ausgeprägtes Stadium



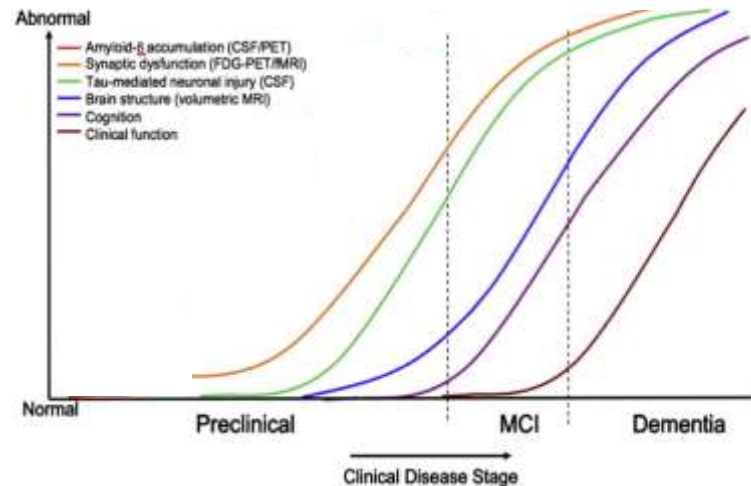
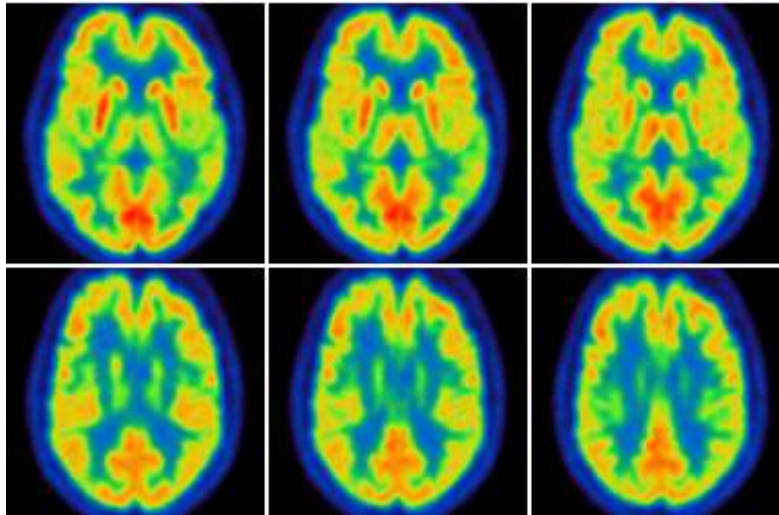




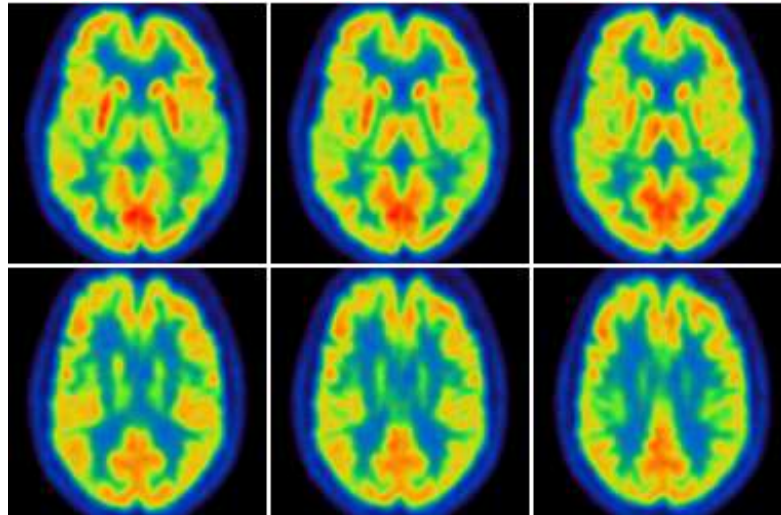
Untersucherunabhängige Befundung durch pixelweisen Vergleich mit Normkollektiven



Frühsymptomatisch
(^{18}F FDG)

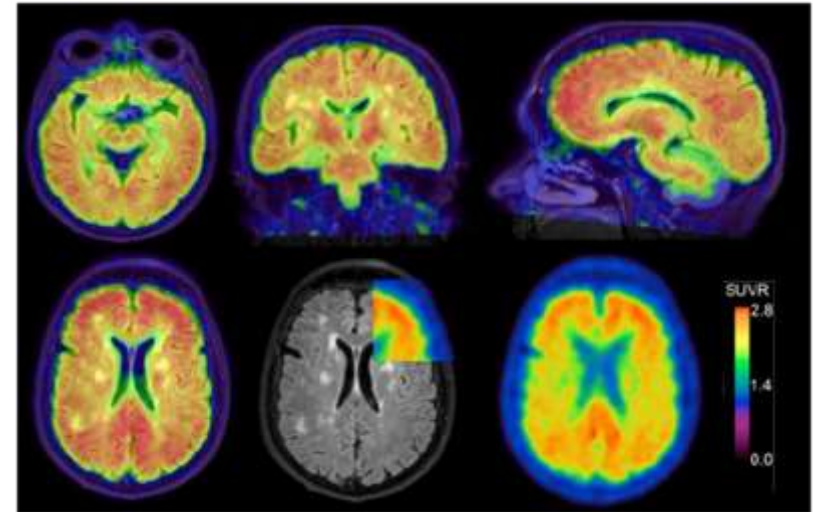


Frühsymptomatisch
(^{18}F FDG)

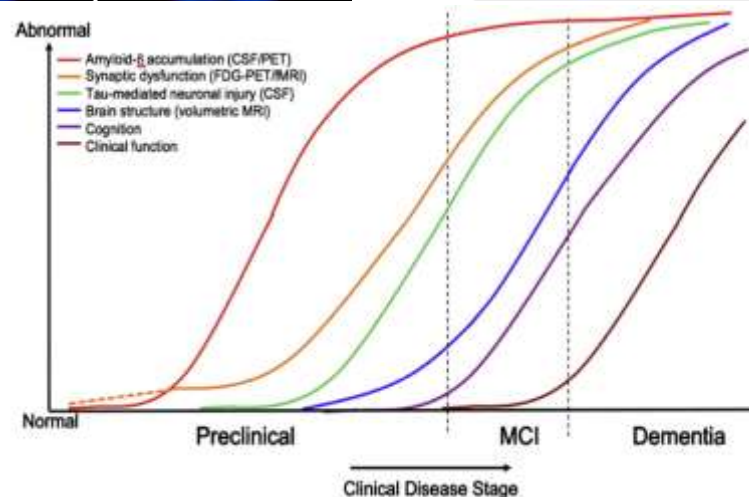


Neuronale Funktion

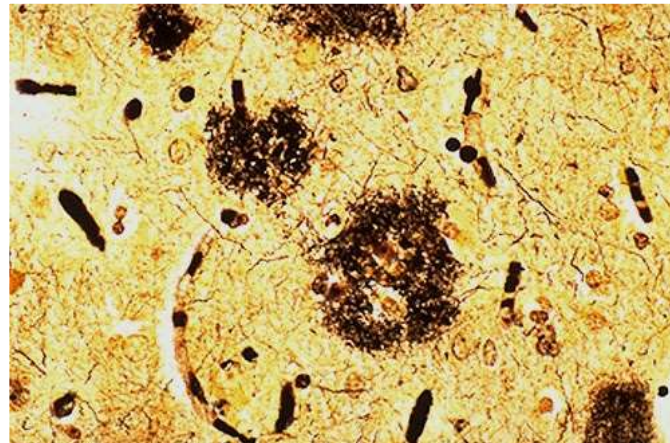
Präsymptomatisch
(^{18}F Flutemetamol)



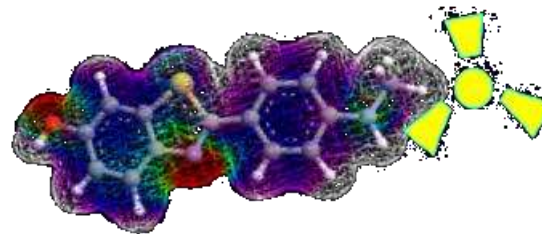
Fibrilläre β -Amyloid
Deposition:



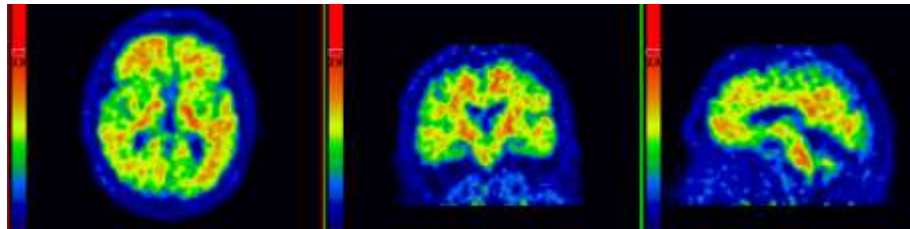
- Schlüsselpotein der AD Pathogenese?
- Verfügbare Radiotracer
 - ^{11}C -PIB
 - ^{18}F -Florbetaben
 - ^{18}F -Florbetapir
 - ^{18}F -Flutemetamol
 - ^{18}F -AZD4694



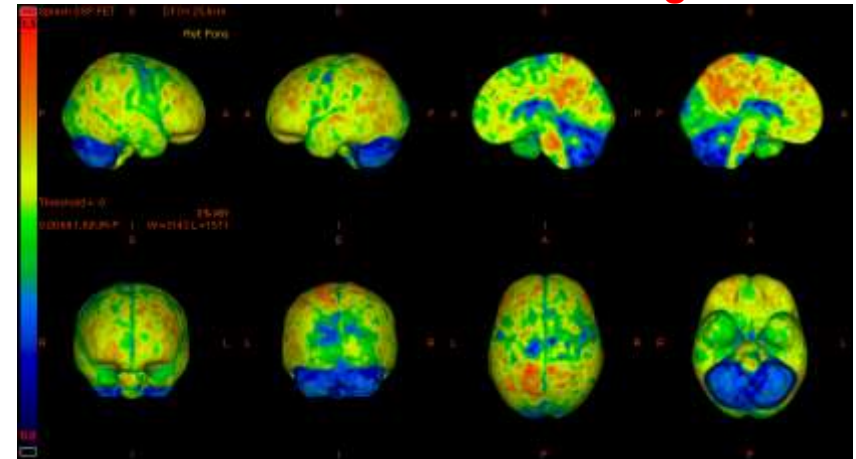
Amyloid-Plaques



Original PET scan



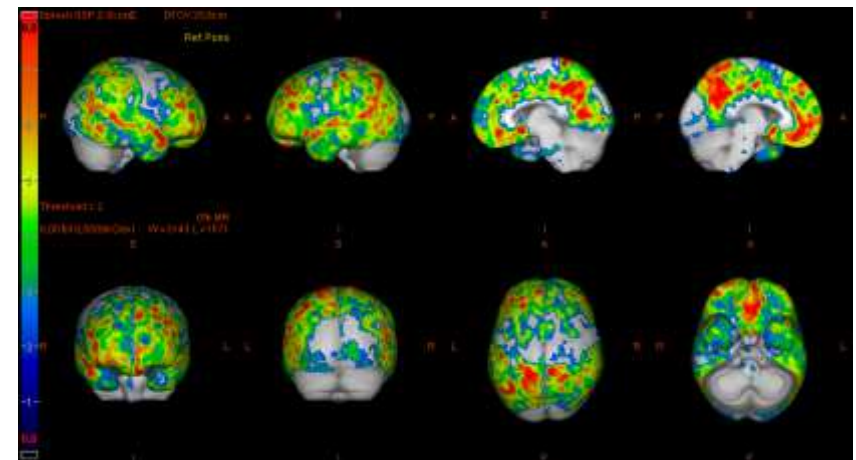
3D SSP of SUVR image



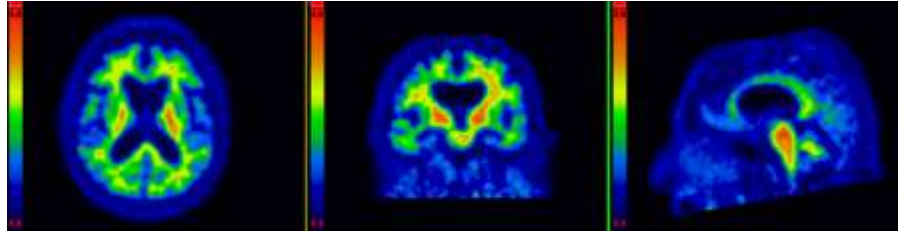
SUVr normalized to pons

Cortical region	Patient	Normal	Z-score
Prefrontal R	0,73	0,46	5,98
Prefrontal L	0,79	0,45	6,87
Sensorimotor R	0,62	0,49	2,58
Sensorimotor L	0,69	0,49	4,05
Occipital R	0,70	0,51	3,39
Occipital L	0,66	0,51	3,04
Parietal R	0,76	0,45	6,96
Parietal L	0,79	0,44	7,38
Anterior Cingulate R	0,81	0,49	5,65
Anterior Cingulate L	0,90	0,53	6,27
Precuneus PostCing R	0,87	0,50	7,96
Precuneus PostCing L	0,92	0,52	8,86
Temporal Lateral R	0,77	0,49	6,24
Temporal Lateral L	0,80	0,48	6,23
Temporal Mesial R	0,58	0,52	1,63
Temporal Mesial L	0,61	0,51	2,10
Cerebellum	0,33	0,40	-1,60
Pons	1,00	1,00	0,00

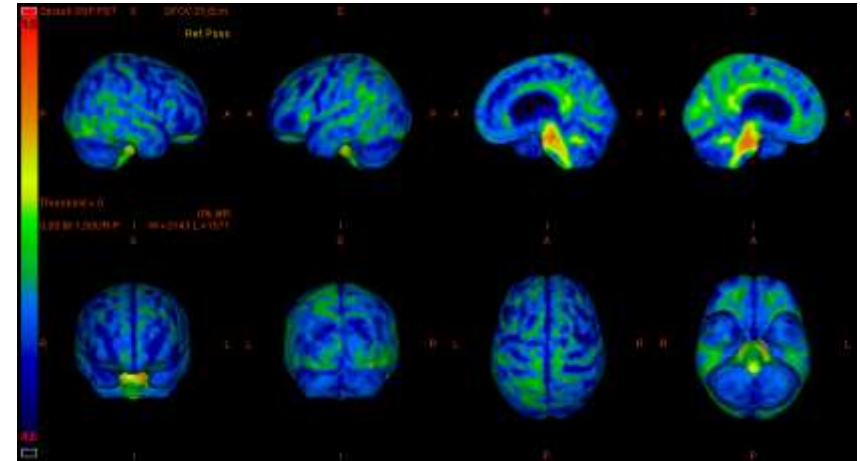
3D SSP Z-scores



Original PET scan



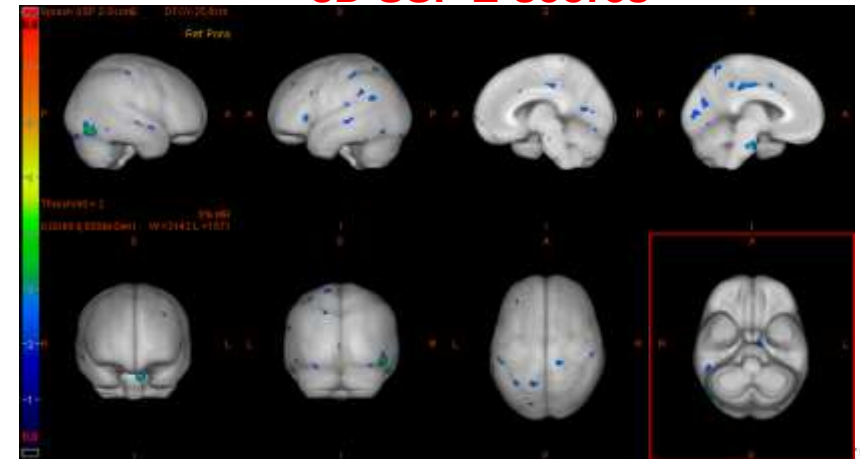
3D SSP of SUVR image



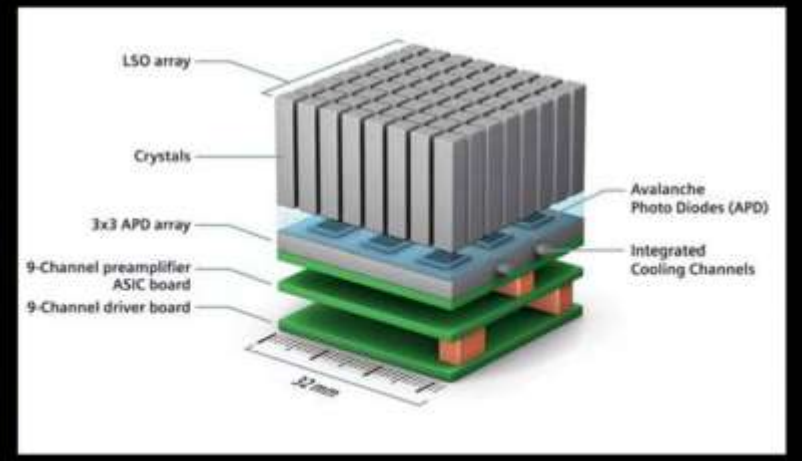
SUVr normalized to pons

Cortical region	Patient	Normal	Z-score
Prefrontal R	0,34	0,46	-2,59
Prefrontal L	0,36	0,45	-1,98
Sensorimotor R	0,36	0,49	-2,36
Sensorimotor L	0,38	0,49	-2,15
Occipital R	0,45	0,51	-1,11
Occipital L	0,46	0,51	-0,81
Parietal R	0,37	0,45	-1,86
Parietal L	0,41	0,44	-0,75
Anterior Cingulate R	0,41	0,49	-1,44
Anterior Cingulate L	0,50	0,53	-0,44
Precuneus PostCing R	0,44	0,50	-1,18
Precuneus PostCing L	0,52	0,52	0,07
Temporal Lateral R	0,45	0,49	-0,96
Temporal Lateral L	0,43	0,48	-1,05
Temporal Mesial R	0,39	0,52	-3,21
Temporal Mesial L	0,42	0,51	-2,12
Cerebellum	0,33	0,40	-1,50
Pons	1,00	1,00	0,00

3D SSP Z-scores



- Eine Anmeldung, eine Untersuchung, ein Befund, eine Rückfrage, eine Befund- demonstration
- Zeitersparnis für Patient und befundende Ärzte
- Verkürzung der Liegedauer (>> DRG)
- Der Kliniker versteht den Vorteil der multimodalen Bilddiagnostik
- Verbesserung von Sensitivität und Spezifität in der onkologischen Diagnostik

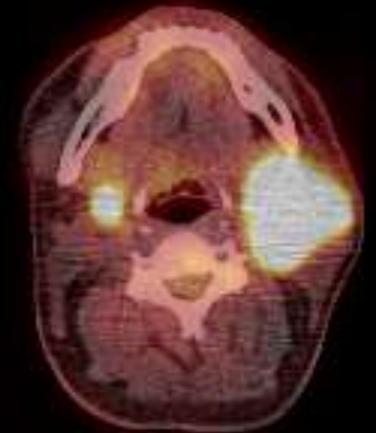
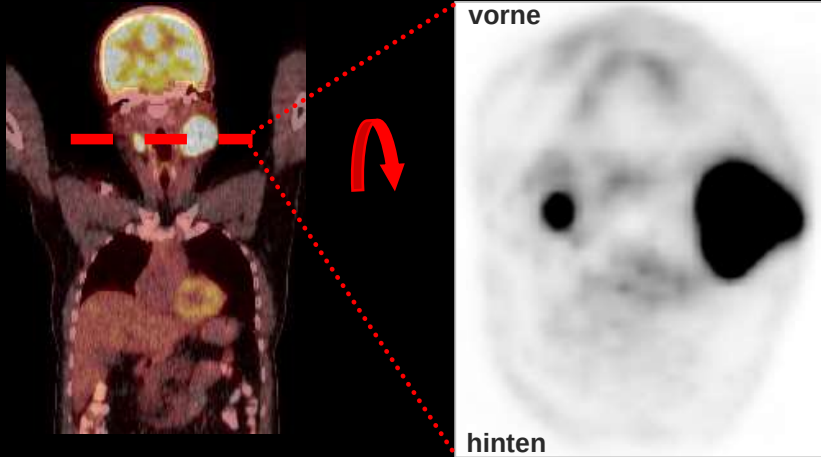


(Siemens Biograph mMR)

FDG-PET (Metabolismus)

CT
(low dose)

Fusion
FDG-PET CT



B) PET-MR:

FDG-PET (Metabolismus)

MRI
(Struktur)

Fusion
FDG-PET MR

