Glioblastoma work-up and collaboration with the nuclear medicine department

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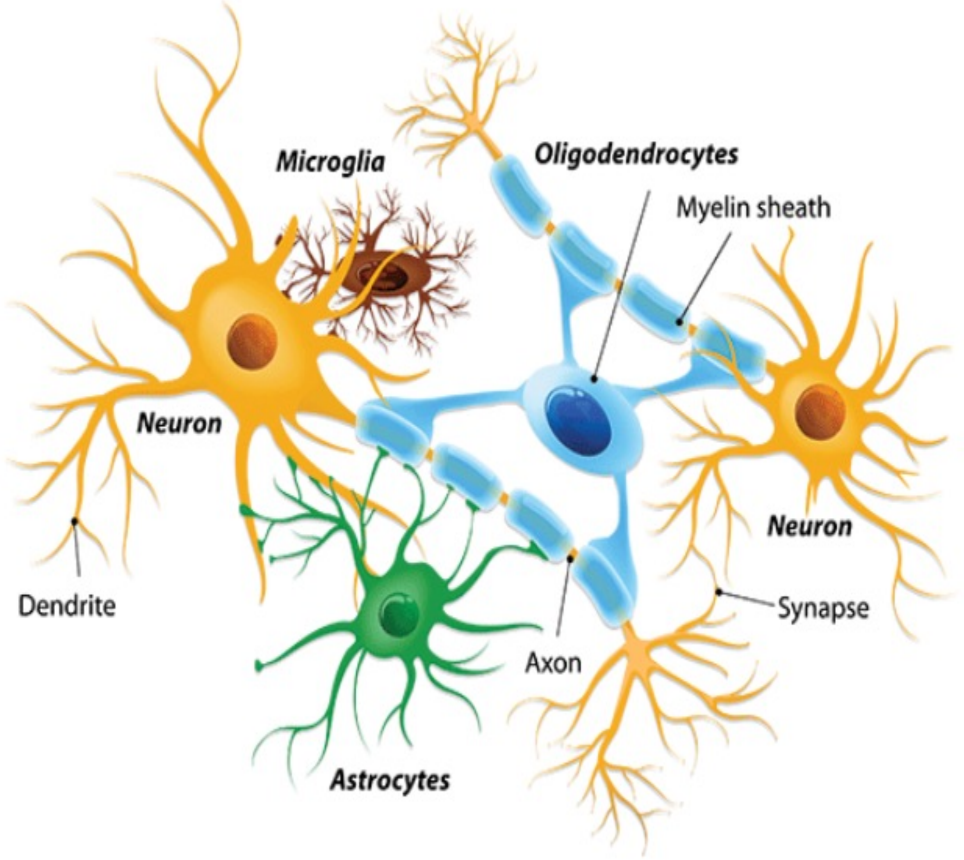
Introduction

- Glial cells = supportive cells in the brain
  - 3 types
    - Astrocytes
    - Oligodendrocytes
    - Microglia

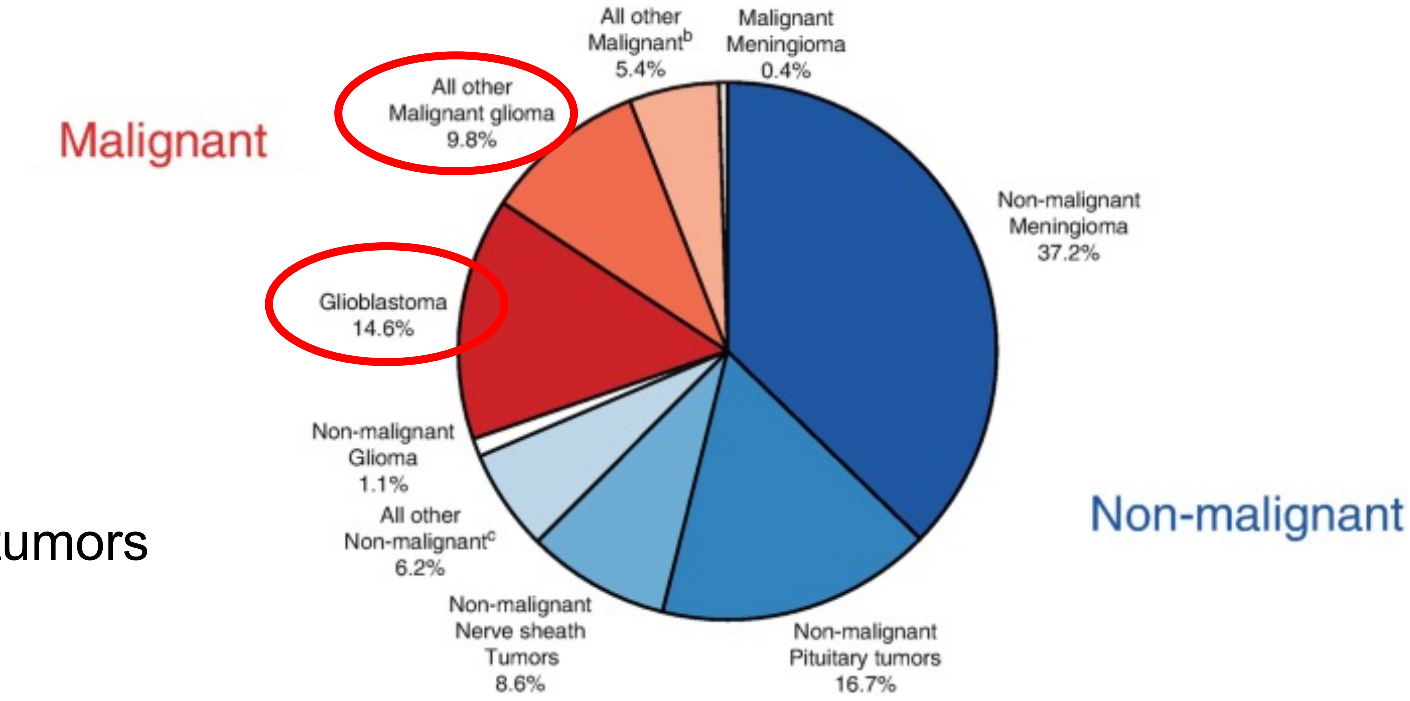
→ ± 90% of brain



- Glioma is a neoplastic transformation of glial cells

→ Refers to a group of tumors

Epidemiology



- 25% of all brain tumors

  = 80% of all malignant brain tumors

- Incidence of glioma in Belgium: ± 7 per 100.000 inhabitants

→ 600-700 new patients per year

https://doi.org/10.1007/978-3-030-69170-7_1

Glioma classification

- WHO classification 2021: 3 grades (2-4) based on molecular markers
- Grade 2: ‘diffuse’ Astrocytoma/Oligodendroglioma
- Grade 3: ‘anaplastic’ Astrocytoma/Oligodendroglioma
- Grade 4: Astrocytoma/Glioblastoma

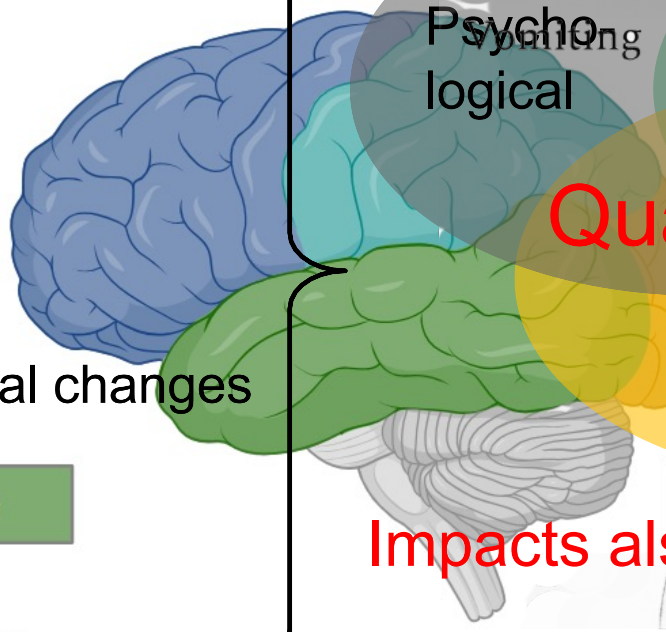
Prognosis ↓

Symptomatology

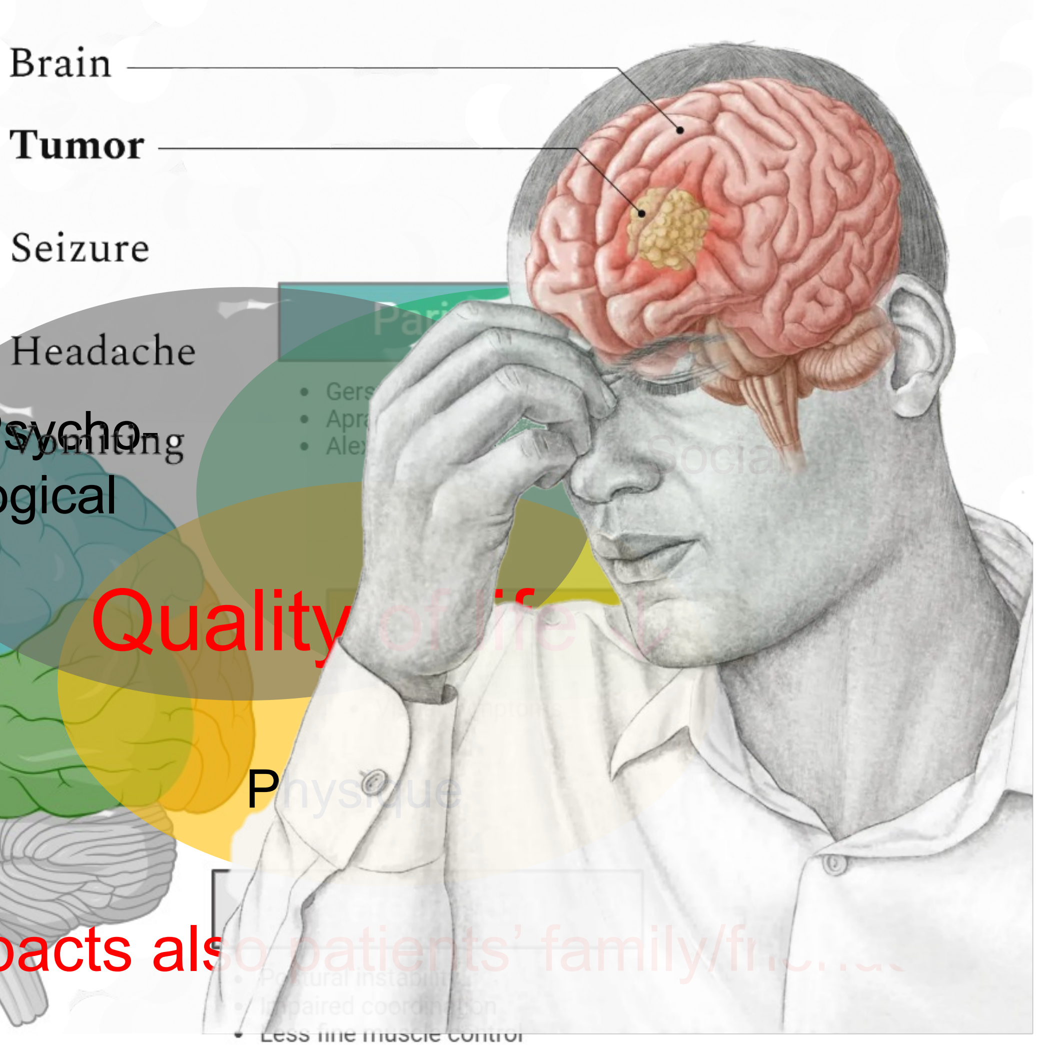
2. Symptoms independent from tumor location
3. Neurological symptoms dependent on tumor location
   - Different from other tumors in the body

- Headaches
- Epilepsia
- Behavioural changes
- Invalidity

Frontal lobe
- Personality changes
- Loss of motor function
- Speaking difficulties
- Less impulse control
- Inappropriate behaviour



Temporal lobe
- Loss of memory
- Hearing difficulties
- Inability to learn and retain new information
- Language comprehension impaired



Psycho-logical

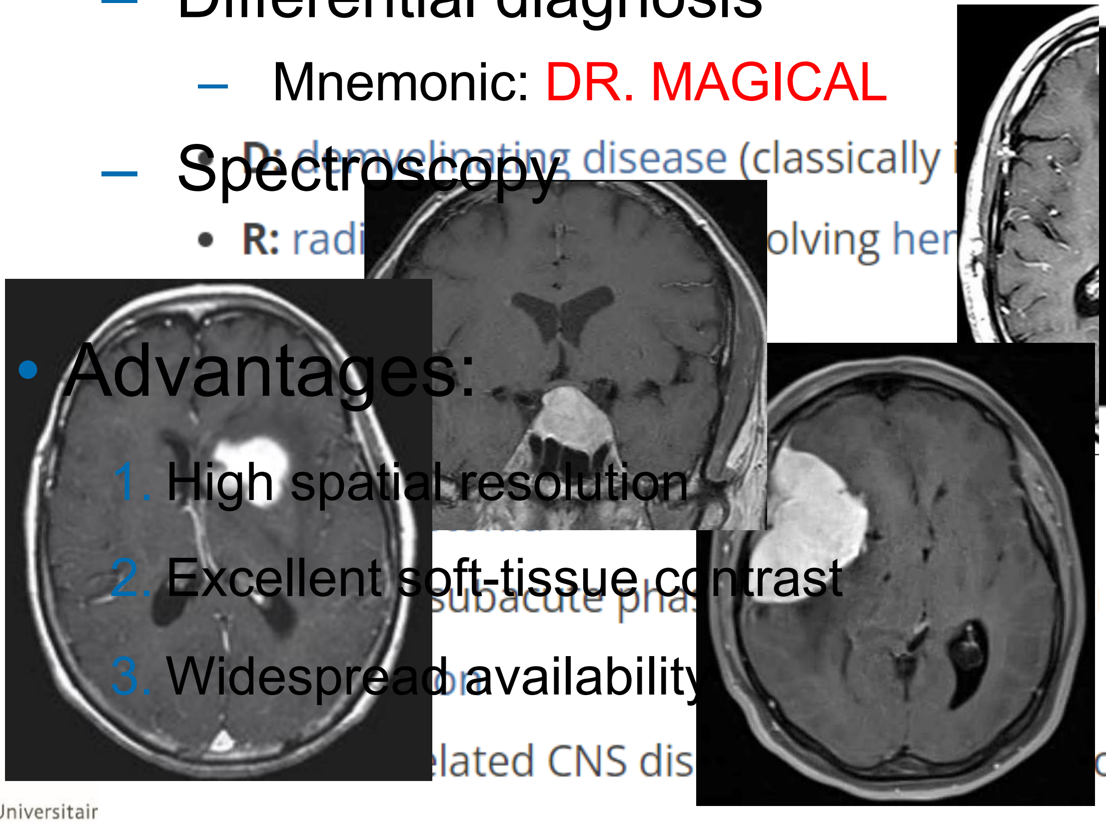
Quality of life

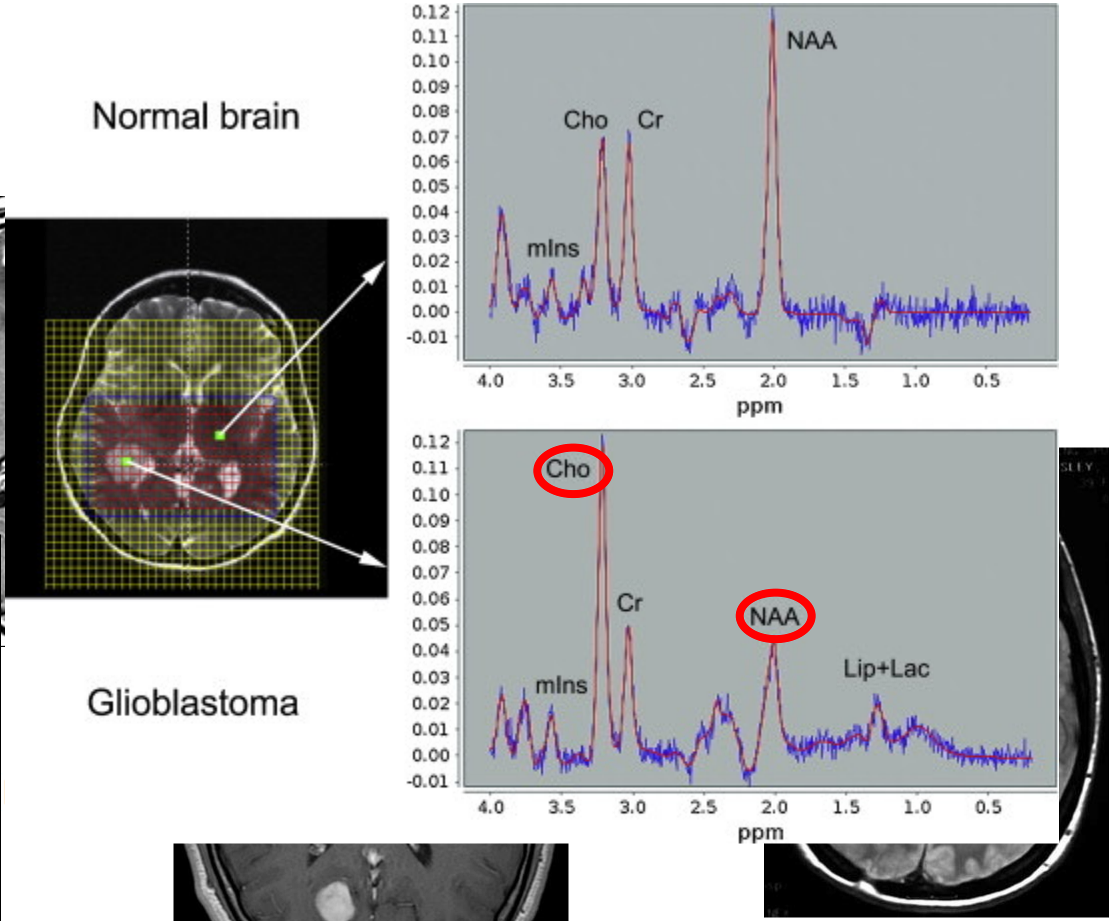
Physique

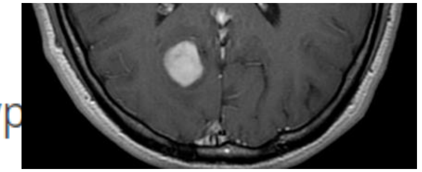
Impacts also patients' family/friends

Diagnosis of glioblastoma

- MRI scan
  - Differential diagnosis
    - Mnemonic: DR. MAGICAL
      - D: demyelinating disease (classically i
      - R: radi … olving her
  - Spectroscopy







- Advantages:
  1. High spatial resolution
  2. Excellent soft-tissue contrast
  3. Widespread availability

subacute pha

lated CNS dis … osis, cryp

- L: lymphoma (this appearance is more common in immunocompromised)

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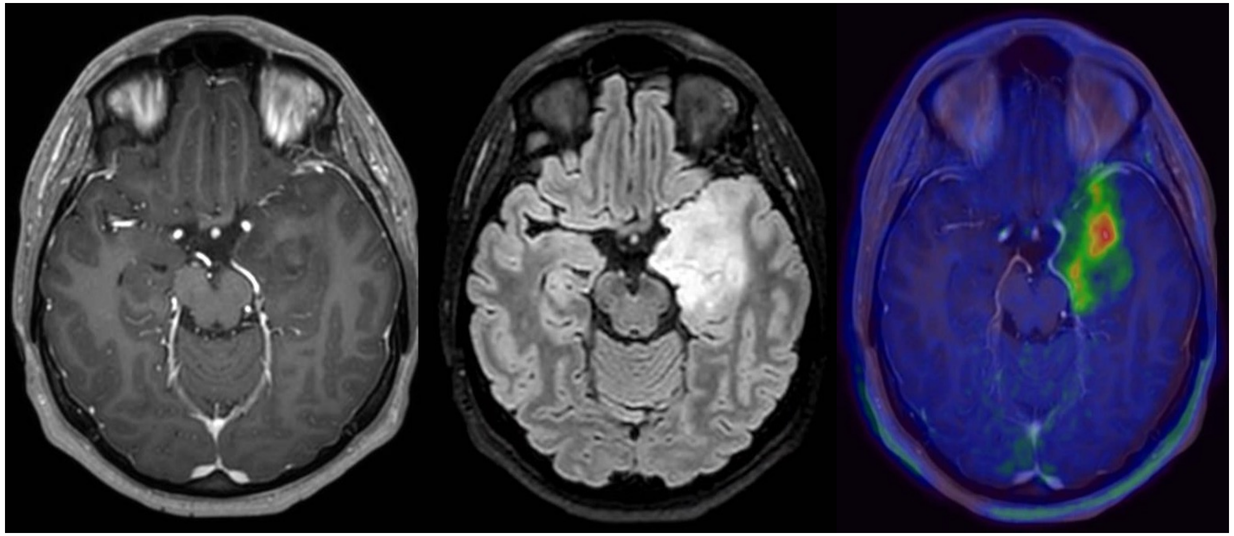
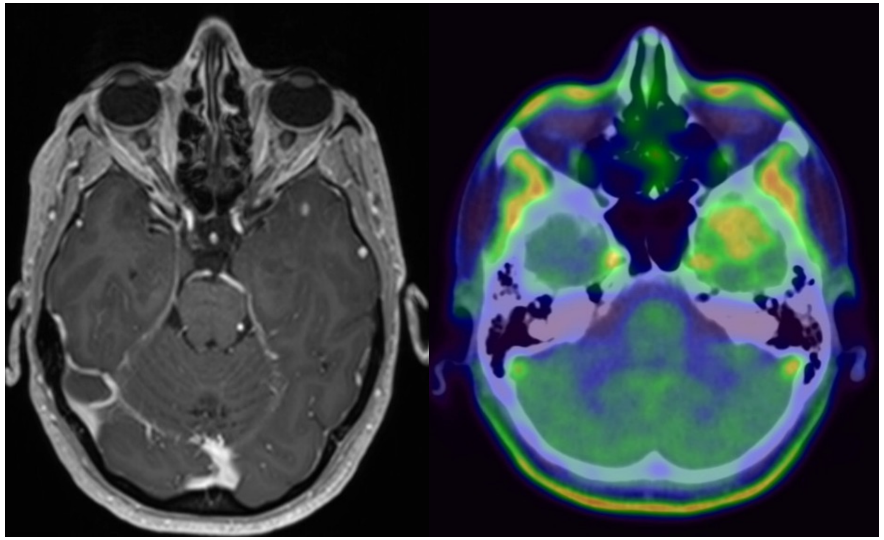
Diagnosis of glioblastoma

- Some cases remain doubtful
    1. No contrast leakage (mostly lower grade gliomas)
    2. Small contrast-enhancing nodule

→ **FET/MET-PET**



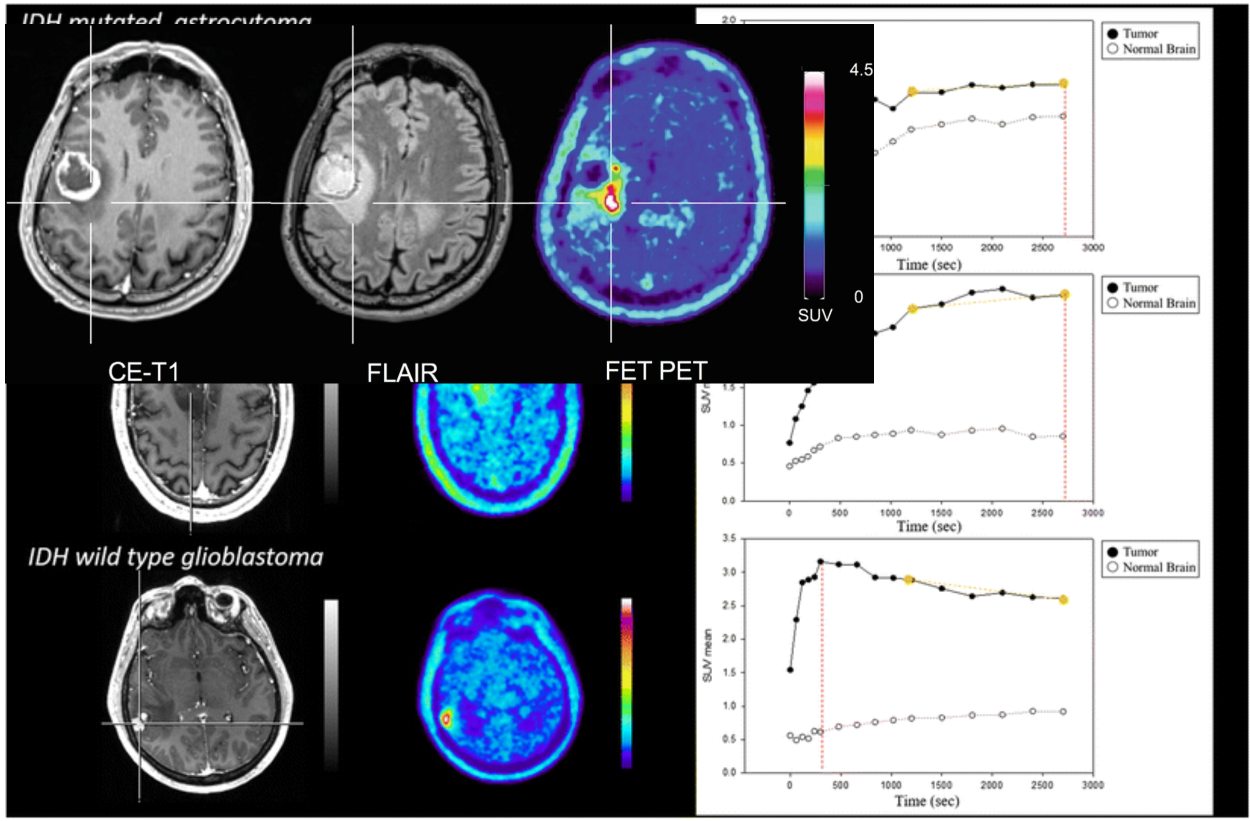


Amino-acid (AA) PET: principles

- Uptake in glioma cells through LAT-1/2 transporter
  - Overexpression in glioma cells

1. Static AA-PET
   - Metabolic Tumor Volume (MTV)
   - Tumor-to-background ratio (TBR)
     - TBRmax
     - TBRmean

2. Dynamic AA-PET
   - Static parameters
   - Slope evaluation (time activity curve)
   - Time-to-Peak (TTP)

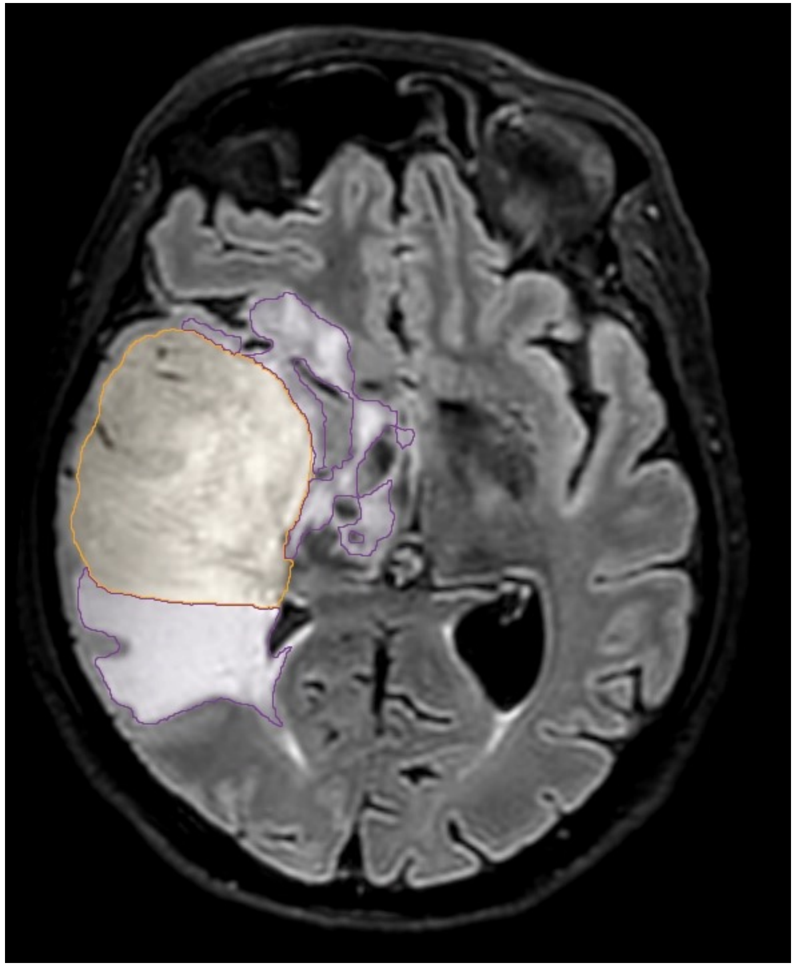


Treatment of glioblastoma

1. Surgical resection
   - Based on pre-operative MRI
     → GOAL: maximal SAFE resection

   - Different subregions in tumor
     1. Necrosis
     2. Contrast-enhancing tumor (CE)
     3. Edema + non-contrastenhancing tumor (NCE)

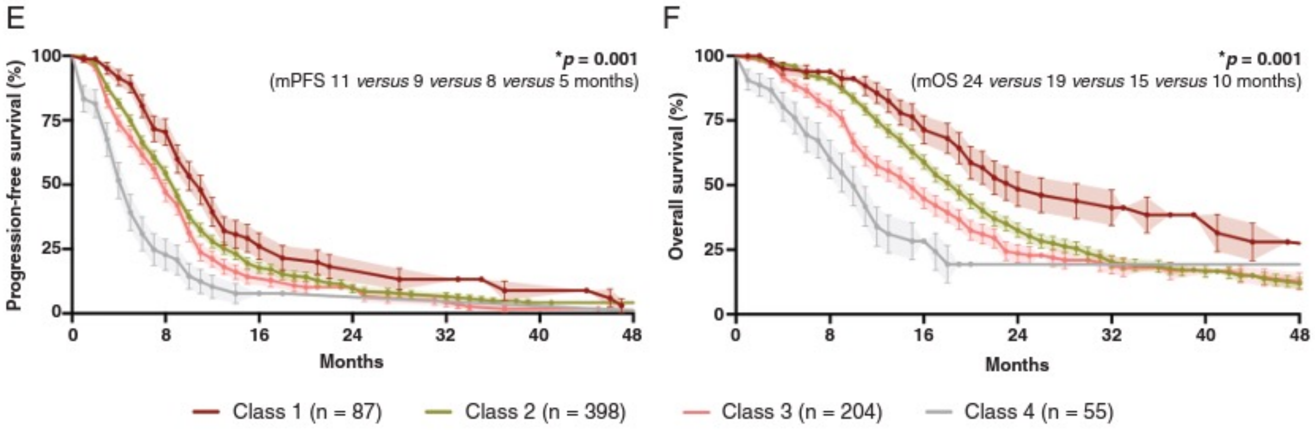
VISIBLE TUMOR



Potential use of AA-PET in neurosurgery

- 1008 primary GBM patients retrospectively analysed
- Based on MR imaging only
- Surgical intervention prognostic?
- 4 subclasses highly prognostic
- Conclusion: lower residual tumor volume (RTV) = higher survival
- Uncertainty about the quantification of NCE
  - No method mentioned in the article

RANO categories for extent of resection in glioblastoma					
Class 1: supramaximal CE resection	**Class 2: maximal CE resection**		**Class 3: submaximal CE resection**		**Class 4: biopsy**
	Class 2A: complete CE resection	*Class 2B: near total CE resection*	*Class 3A: subtotal CE resection*	*Class 3B: partial CE resection*	
0 cm^3 CE + ≤5 cm^3 nCE	0 cm^3 CE + >5 cm^3 nCE	≤1 cm^3 CE	≤5 cm^3 CE	>5 cm^3 CE	No reduction of tumor volume



Karschnia et al. Neuro-oncology, 2022

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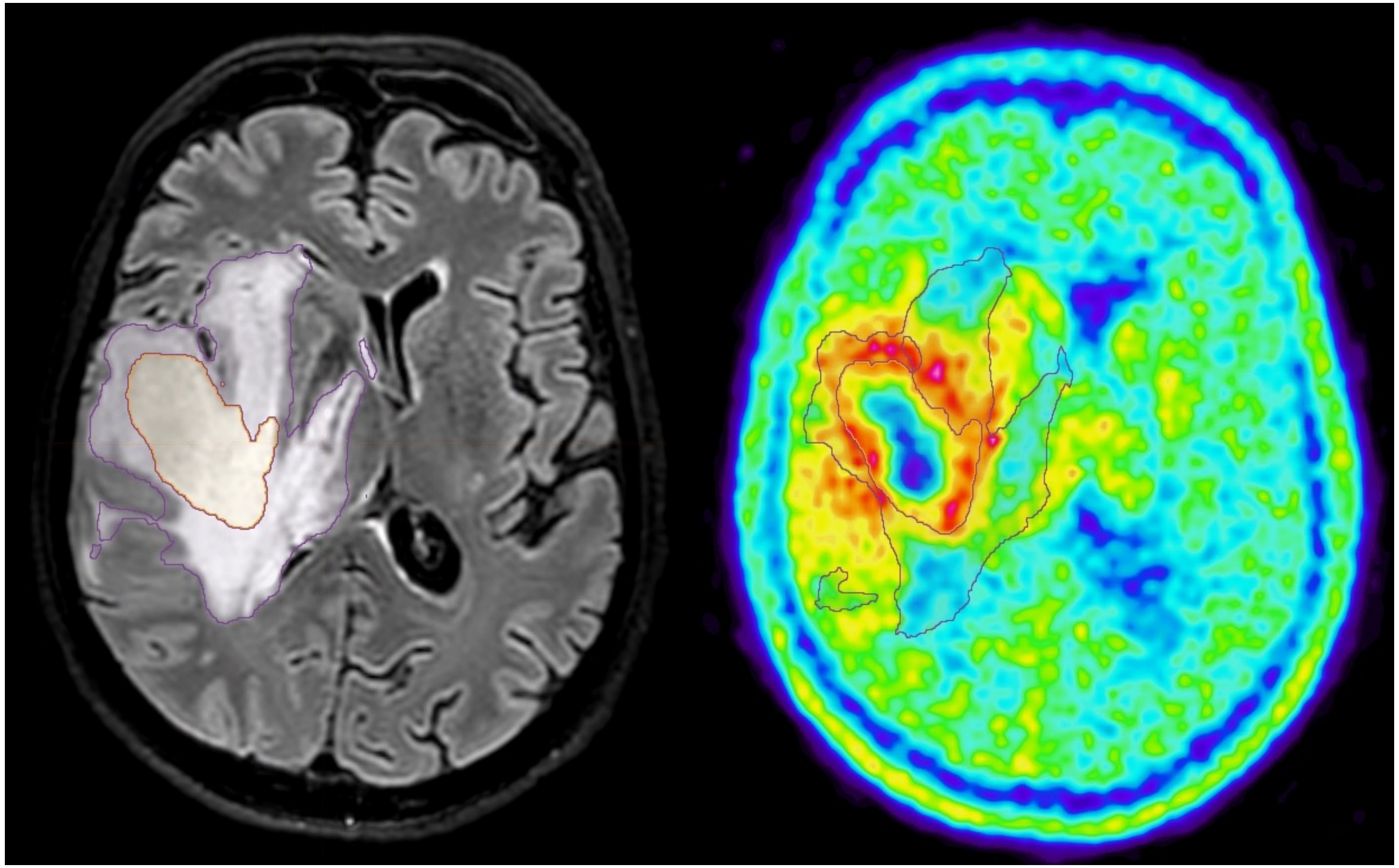
Edema + non-contrastenhancing tumor

→ Contains tumor infiltration

Reminder:
Yellow = Necrosis + CE
Purple = Edema + NCE



Potential use in neurosurgery

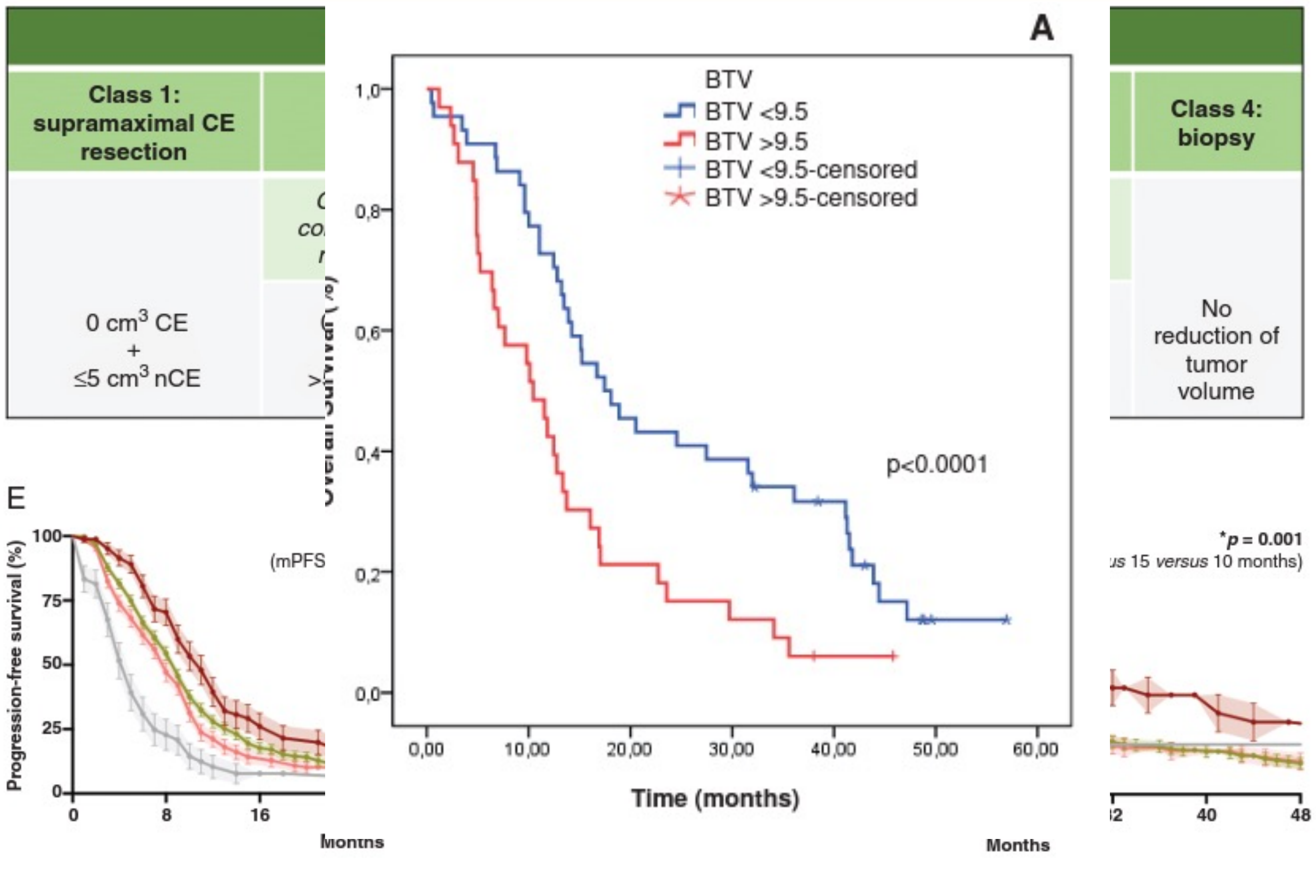
- No information regarding tumoral infiltration in previous trials investigating extent of resection
- MTV before adjuvant treatment highly prognostic

→ Classes should be redefined

with AA-data incorporated

→ Need for prospective studies

with combined PET/MRI evaluation



Suchorska et al., Neurology, 2015

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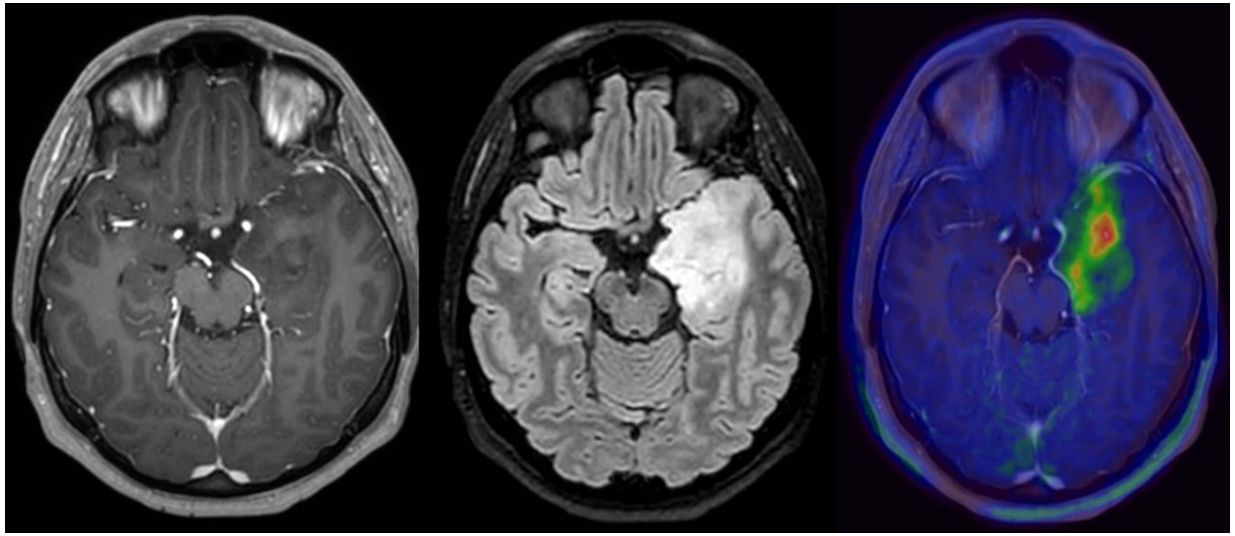
Potential use in neurosurgery

- Biopsy planning
  - Identification of highly malignant foci
  - Particularly of interest in lower lower-grade gliomas



Conclusion: potential use in neurosurgery

1. Guiding surgical resection
   - Higher resection grade = **Higher** survival

     → **Minimize postoperative residual tumor volume**

CAVE

- Higher postoperative deficits = **worse** prognosis

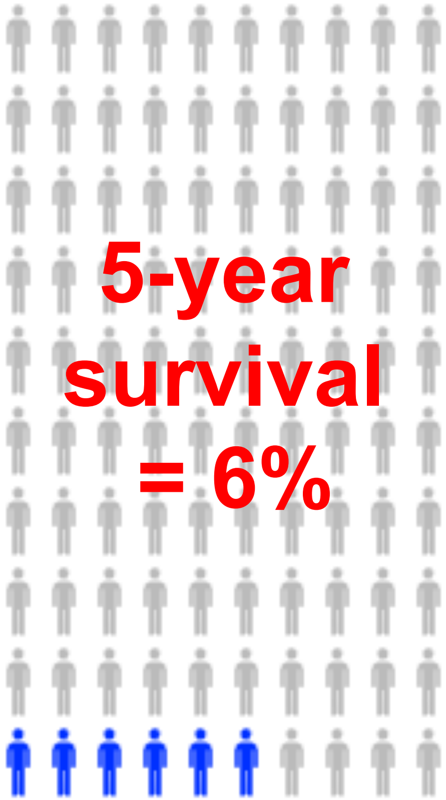
  → **Finding a good balance is essential**

2. Guiding biopsy location
   - Preferably lesion with high PET activity = aggressive portion of tumor

Treatment of glioblastoma
(unchanged since 2005)

1. Surg… …opsy if inope…
   - aim… …esection
2. Con… …chemothera…
   - 6 w…
   - Foll… …apy alone in h…
     - …week chemo and…

5 years



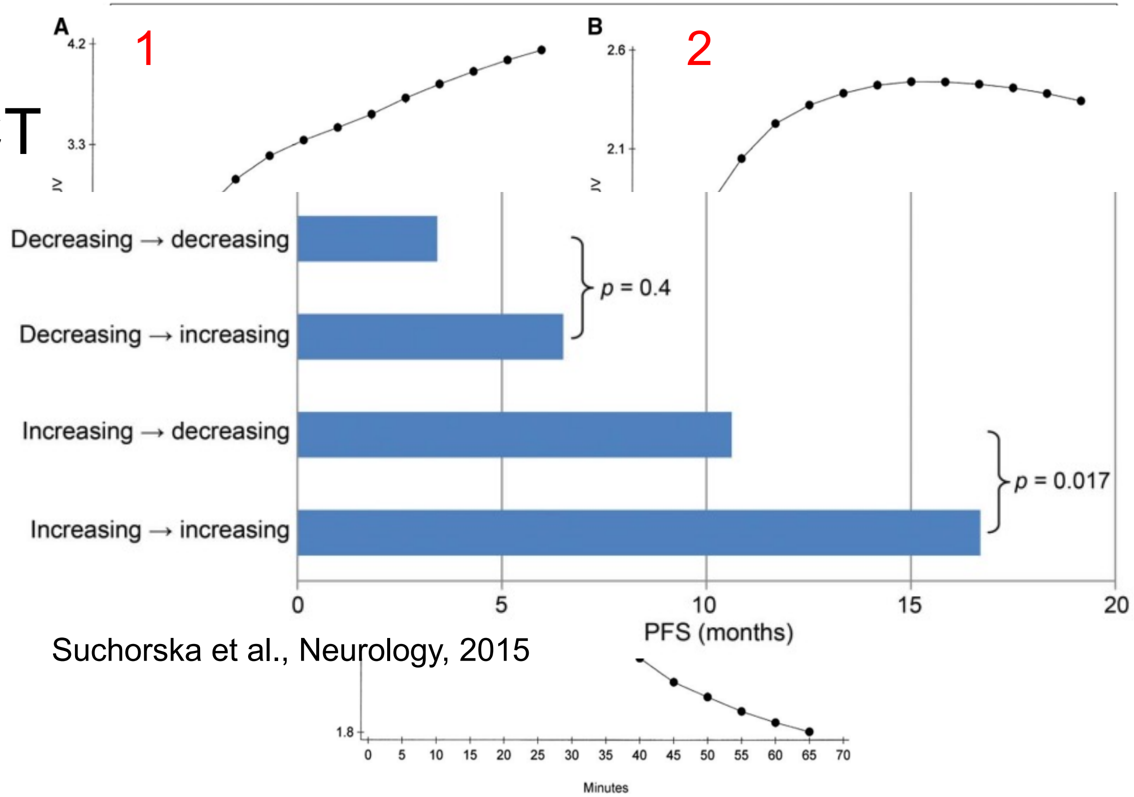
Median… …nths

Prognostication using amino-acid PET

- Response assessment to radiochemotherapy (RCT) vital
  - Allows for adequate patient counseling
  - Although not relevant in glioblastoma, may allow for an earlier therapy adaptation

- Detection of treatment response after RCT
  - Static PET
    - > 10% decrease in TBRmax
    - > 5% decrease in TBRmean

    Longer OS
  - Dynamic PET
    - Type 1/2 activity curve after RCT: longer PFS



Suchorska et al., Neurology, 2015

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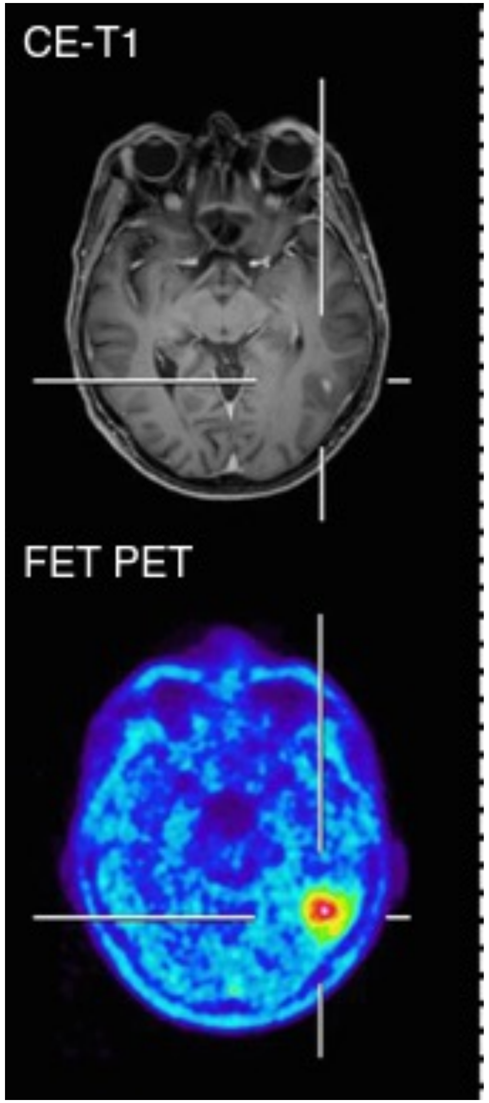
Clinical case 1

- 68 year old patient
- Grade 4 GBM
- Treatment with adjuvant chemotherapy
- Tumor progression?



Use in neuro-oncology: pseudoprogression

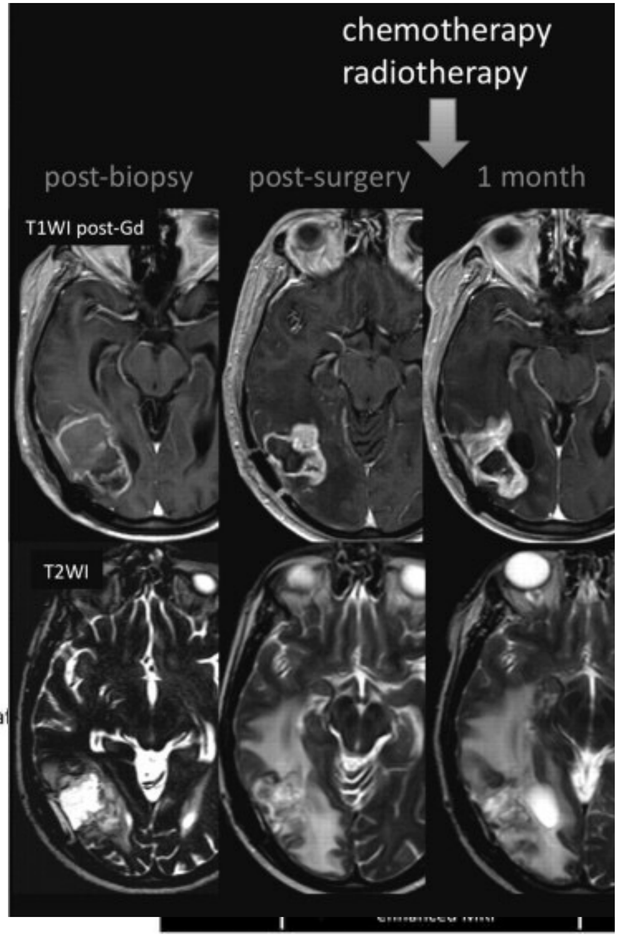
= transient increase of contrast-enhancement (CE) on MRI following anti-tumor treatment

Follow-up MRI will show gradual decrease of CE

- Occurs classically after completion of radiotherapy
  - Mostly within 3 months
  - Might be associated with symptoms

- Immunotherapy
  - Occurs faster after treatment initiation

- **TBRmax < 2.3 = pseudoprogression**
  sens (100%), spec (91%)



Galldiks et al., EJNMMI 2015

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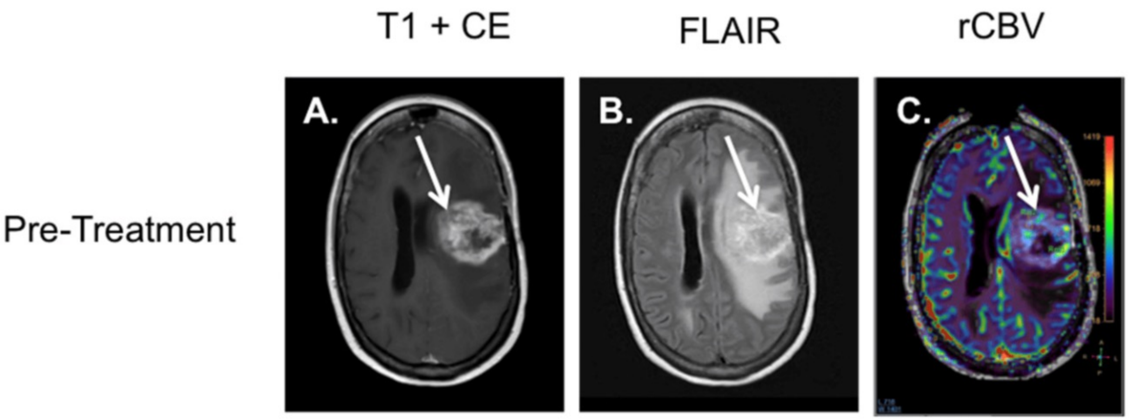
Clinical case 2

- 56 year old patient
- Grade 4 GBM
- Progression after chemo-radiation therapy
- Inclusion in clinical trial
  - Anti-angiogenesis AB + chemotherapy



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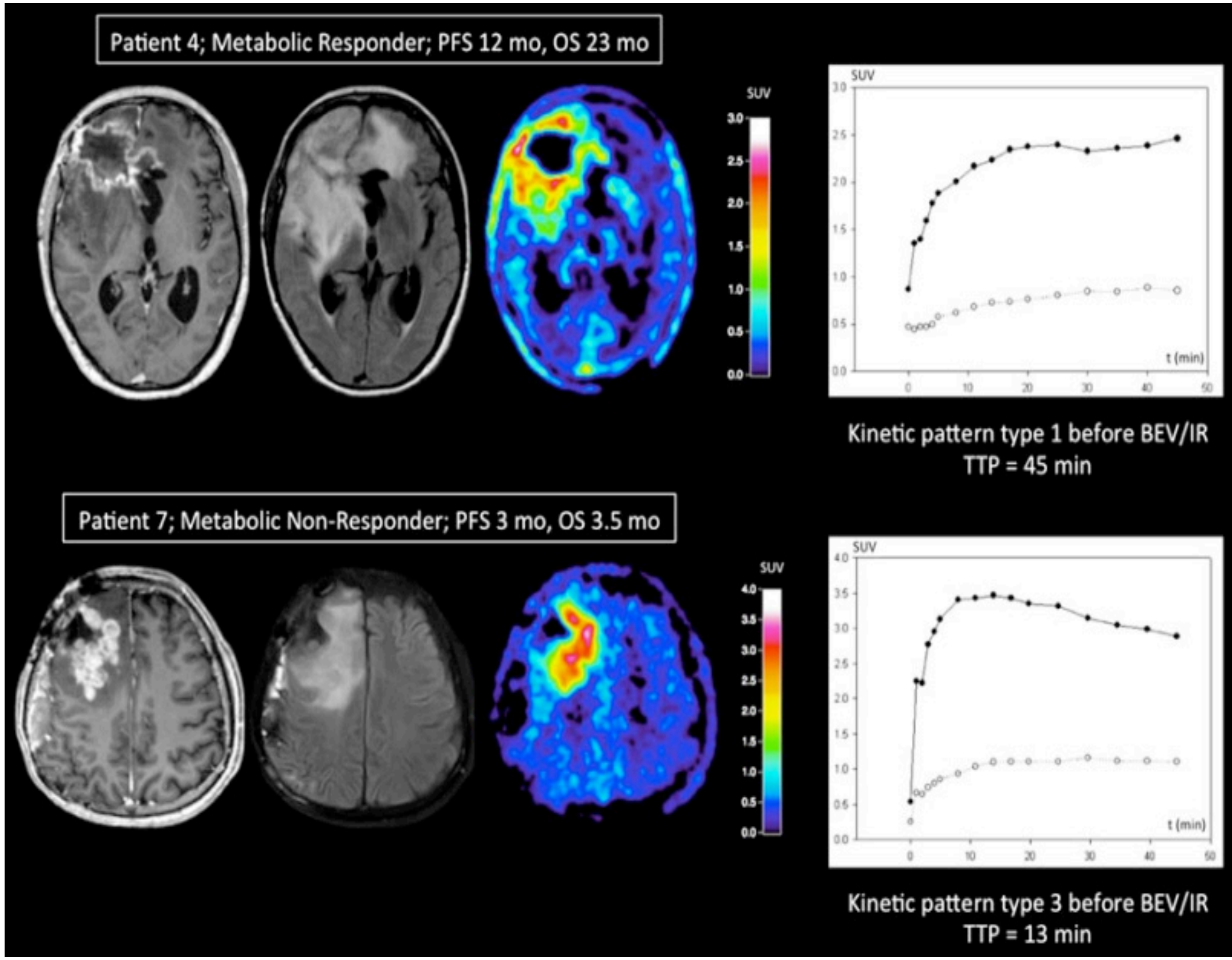
Use in neuro-oncology: pseudoresponse

- Decreased CE on MRI
  - Associated with anti-VEGF therapy
  - Decreased vascular permeability
  - Occurs as fast as 1-2 after treatment initiation
  - Progression as non-enhancing tumor
  - Durable anti-tumor effect in certain patients

- Amino-acid PET
  - Identification of potential responders
    - Type 1 or 2 TAC = better response
  - Detects tumor progression before MRI
    - Prediction of treatment failure



Take home messages

1. Possibility to **distinguish** between tumor grades and types
   → Glioblastoma vs. lower-grade gliomas

2. Amino acid PET may be used for **more accurate** tumor delineation pre-operatively
   → Higher resection grade
   → Longer survival
   → Need for prospective research

3. **Prognostication** of patients with amino acid PET

4. Sensitive to diagnose **treatment-related changes**
   → prevents ineffective treatment from being continued
   OR prevents effective treatment from being halted early

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