Tumor treatment related changes in the CNS

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consequences of treatment on CNS

(sub) acute

infarction
posterior fossa syndrome
radiation reaction
sinus/venous thrombosis by L-Asparaginase
reversible posterior encephalopathy (PRES) tacrolimus/cyclosporine

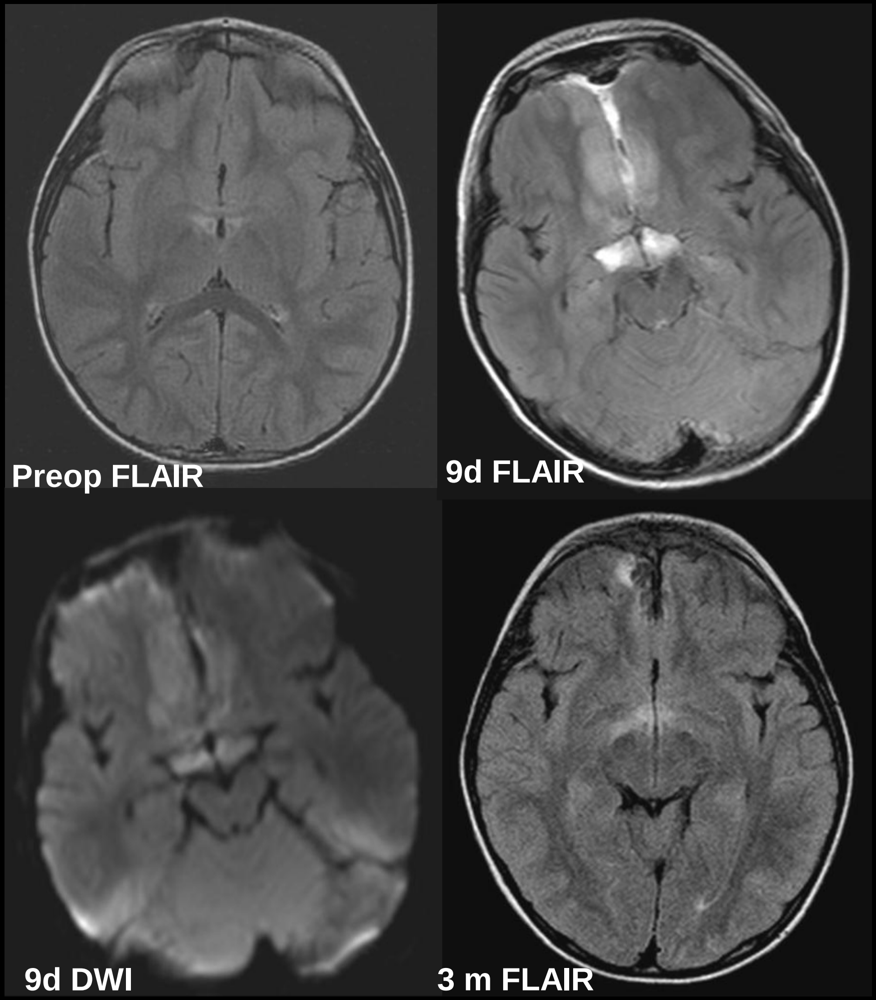
chronic

leukoencephalopathy (radiation/MTX)
degeneration of nuclei
radiation necrosis
intelligence defects
bleeds/cavernomas
growth problems
obesity

second tumors

infarction after surgery

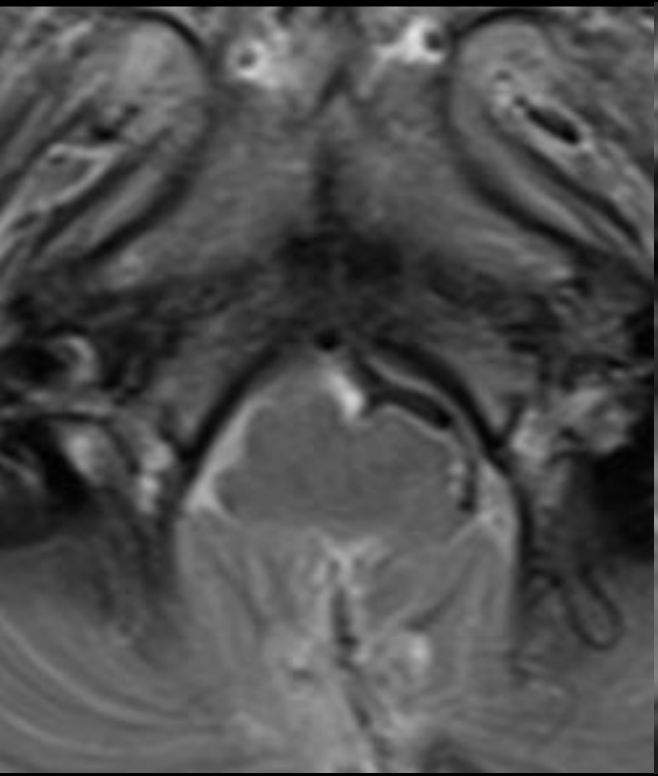
- hazards of resection of chiasmatic gliomas:
- 17% infarcts (n=102 children)
- the younger the worse (3 y vs. 5 y)
- no infarcts after biopsies of whatever technique
- Conclusion:
  if material is needed prefer biopsies and avoid resections



hypertrophic olivary degeneration

- disturbance of the connection: nucleus ruber – nucleus dentatus – nucleus olivaris inferior (Guillain-Mollaret-triangle)
- scarce literature and rare acc. to literature
- etiology:
  - trauma
  - idiopathic
  - surgery in the posterior fossa

HOD



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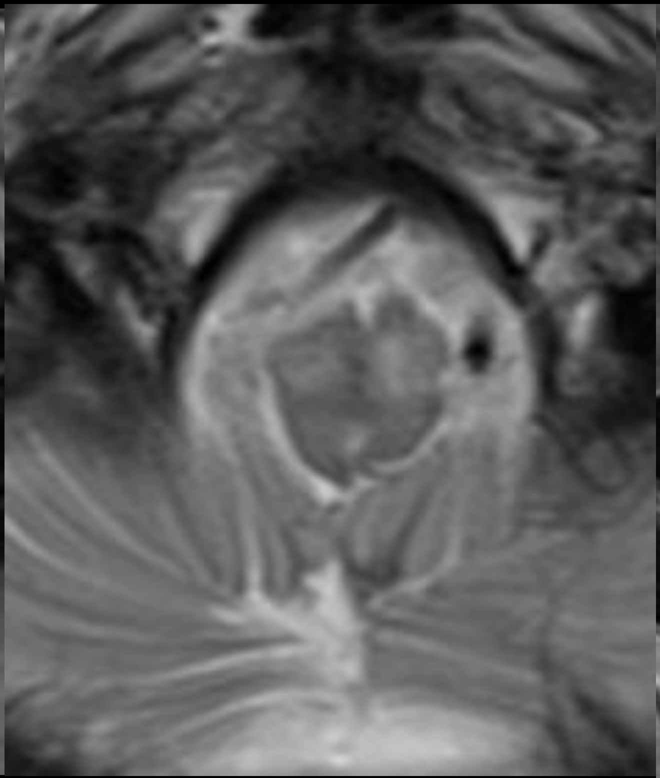

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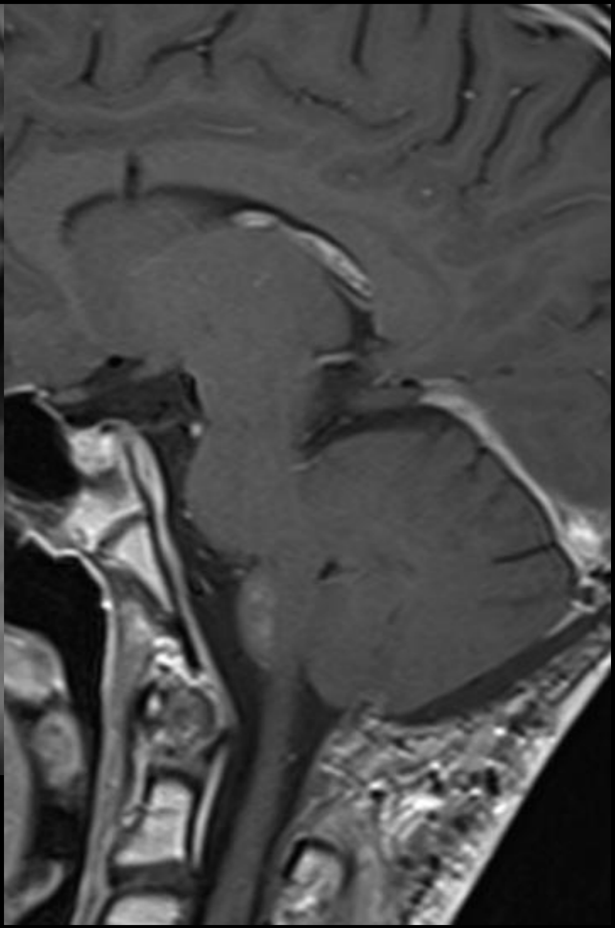


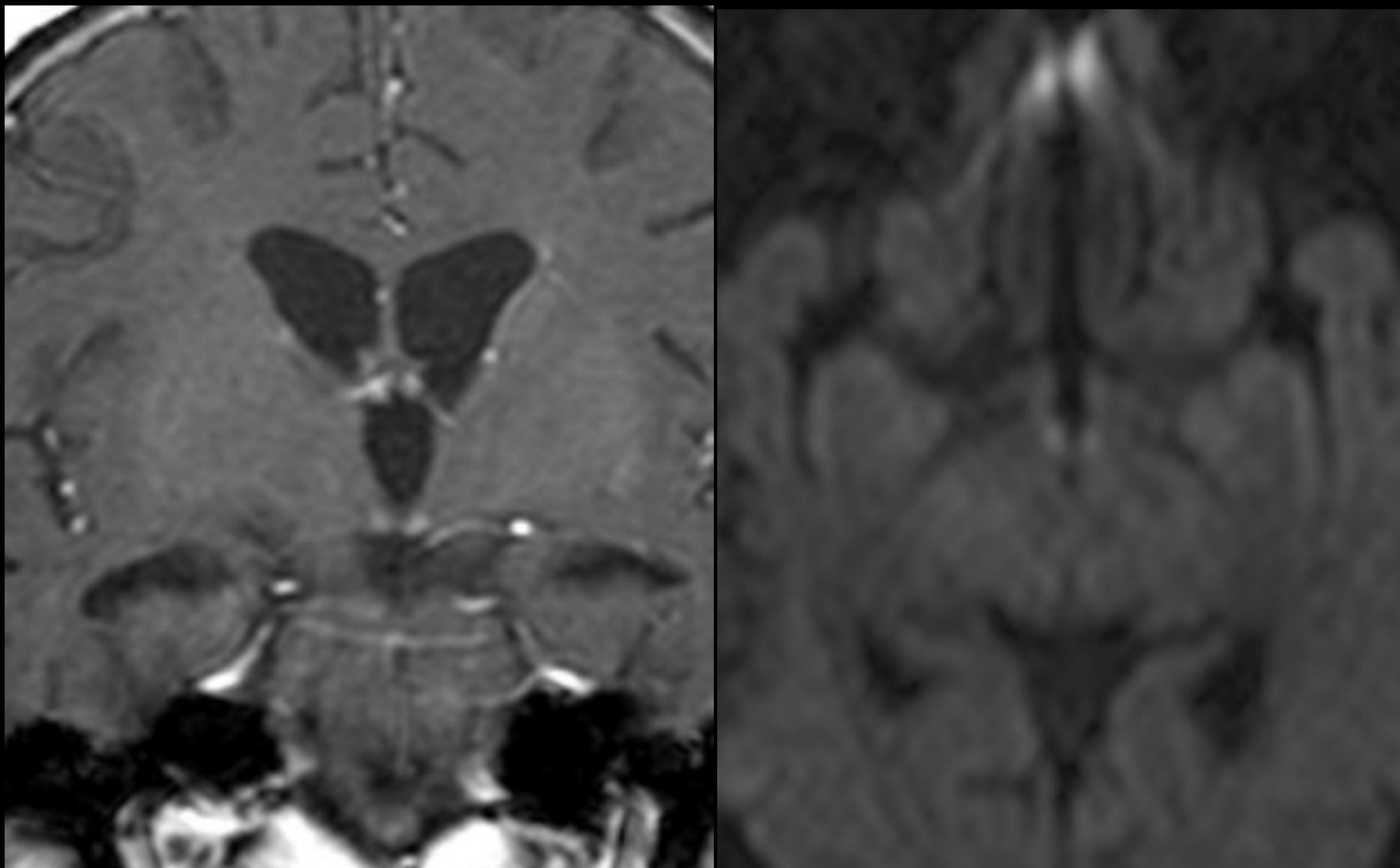
Wernicke disease

- 16 y old girl with a DIPG after irradiation and under TMZ
- sudden loss of conciousness
- artificial ventilation
- tumor progression suspected

- B1 level was reduced, however, on substitution no complete recovery was achieved

Wernicke disease

Wernicke disease



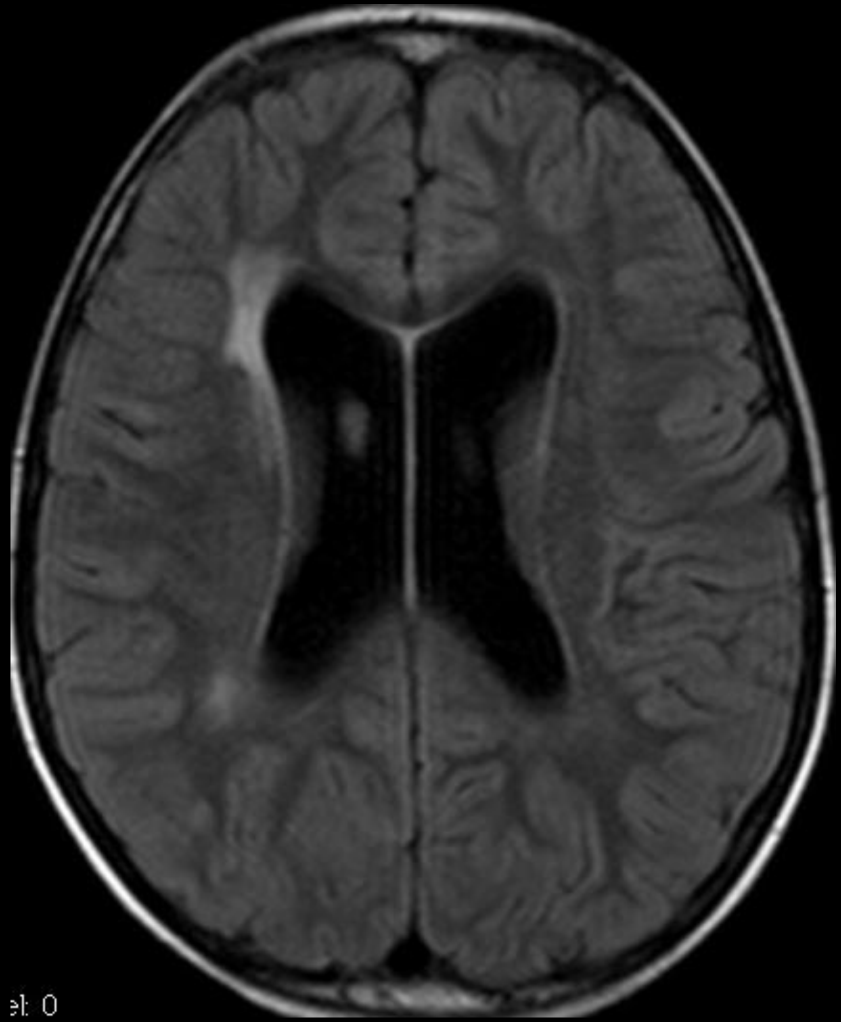
leukoencephalopathy

- after irradiation especially whole brain irradiation
- after MTX i.v. oder i.th., especially if after irradiation
- importance for brain function?
- classification acc. to Fazekas:

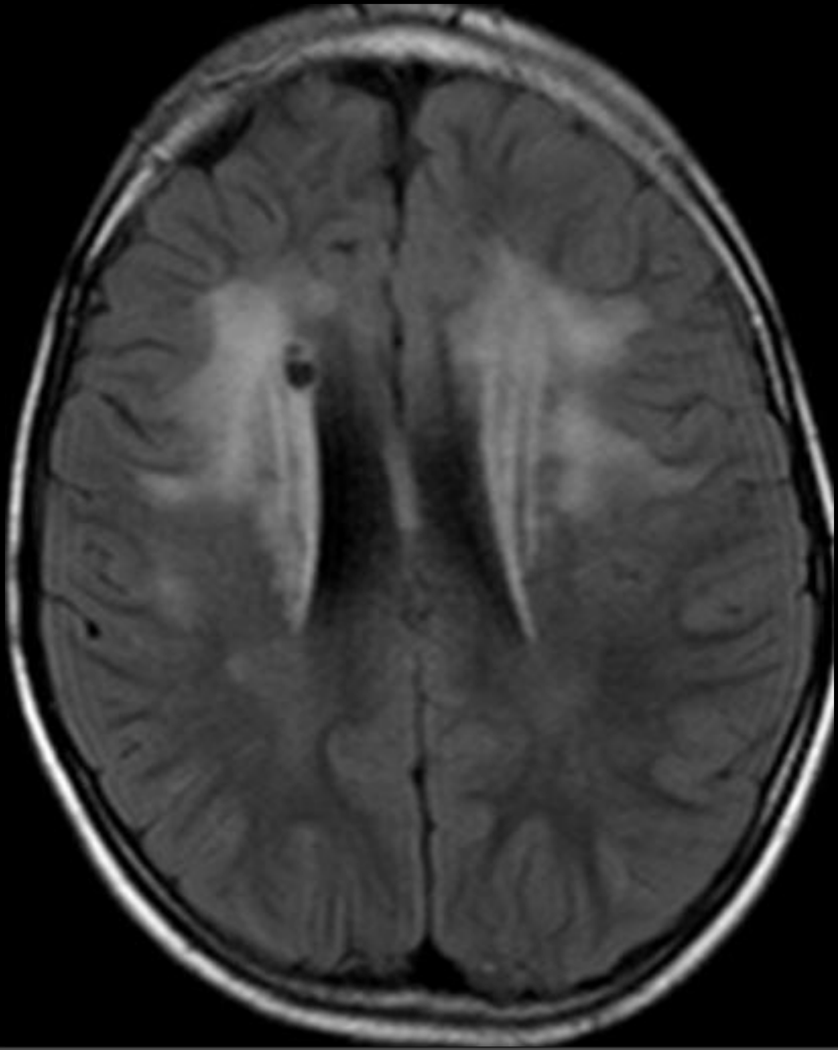
grade 0	normal
grade I	punctated
grade II	confluent
grade III	largely confluent

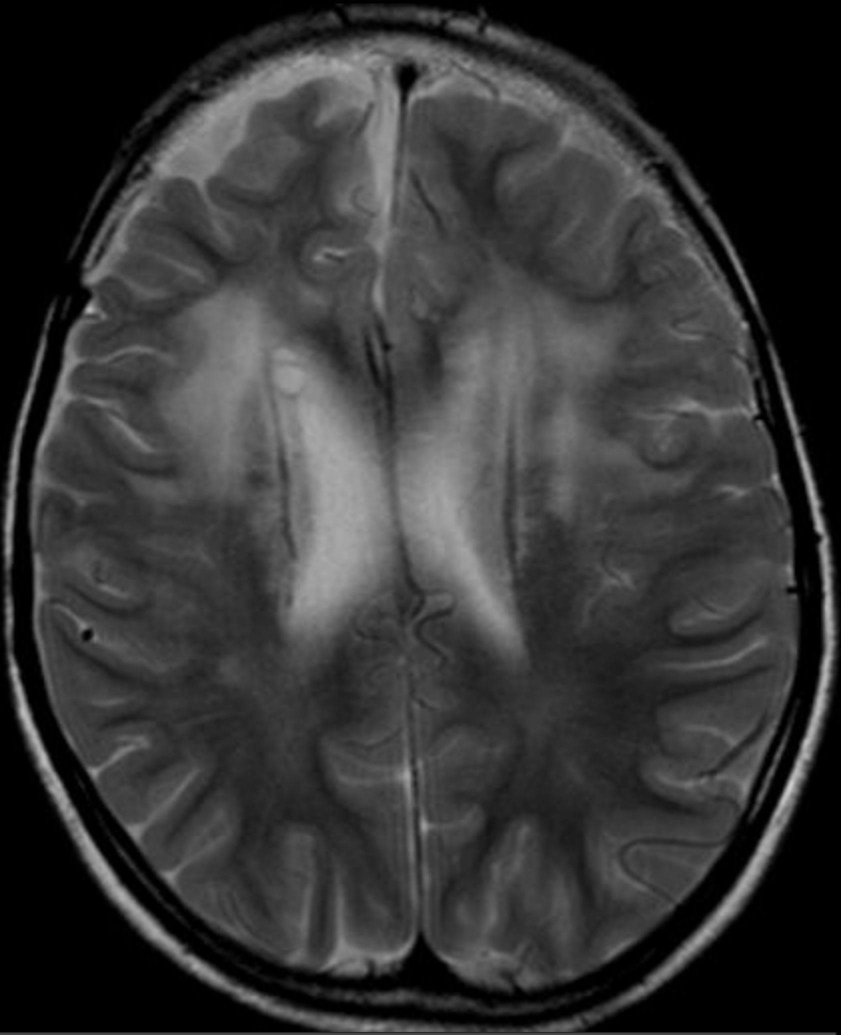
Fazekas et al. Europ Neurol 1989; 33: 169

LEP grade I

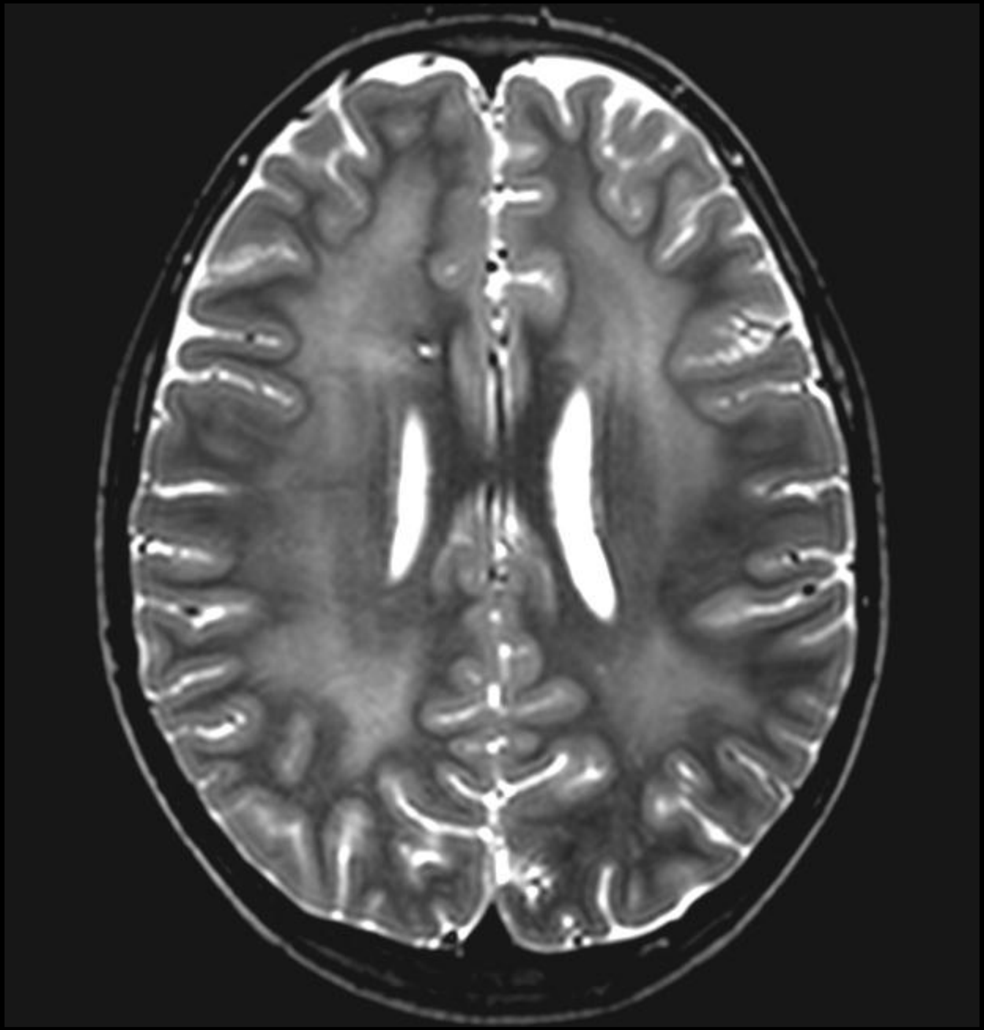


LEP grade II





LEP grade III



MTX LEP in MB

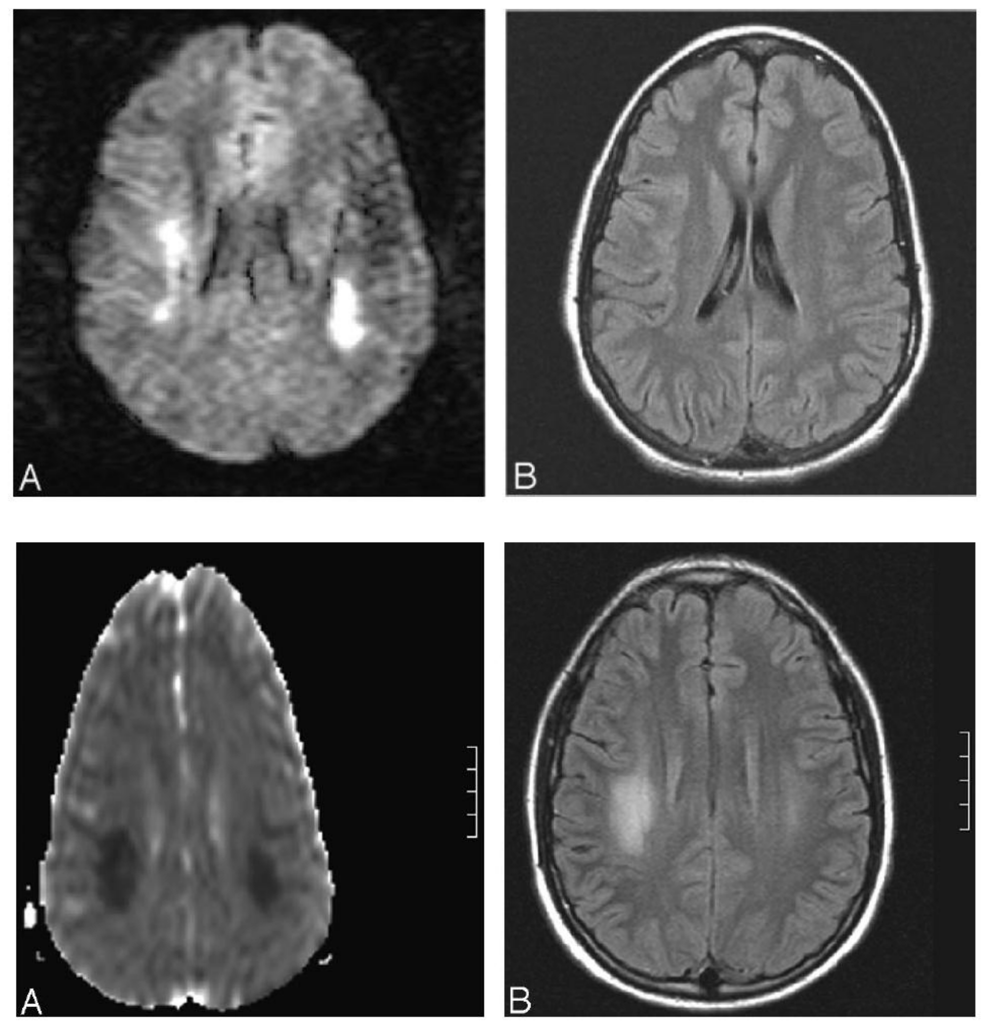
- 36 children below 3 y at the time of diagnosis:
  - 35 i.v. MTX (10-165 g/m2 cum. dose)
  - 21 i.ventr. MTX (20-102 mg cum. dose)
  - 17 CNS irradia. (18-35 gy)
- sign. correlation of intraventr. MTX dose and LEP ($p<0,01$)
- no correlation to IQ
- maximum after about 1 year
- reduction in 50% within 2-3 years

Rutkowski et al: NEJM 2005; 10: 978

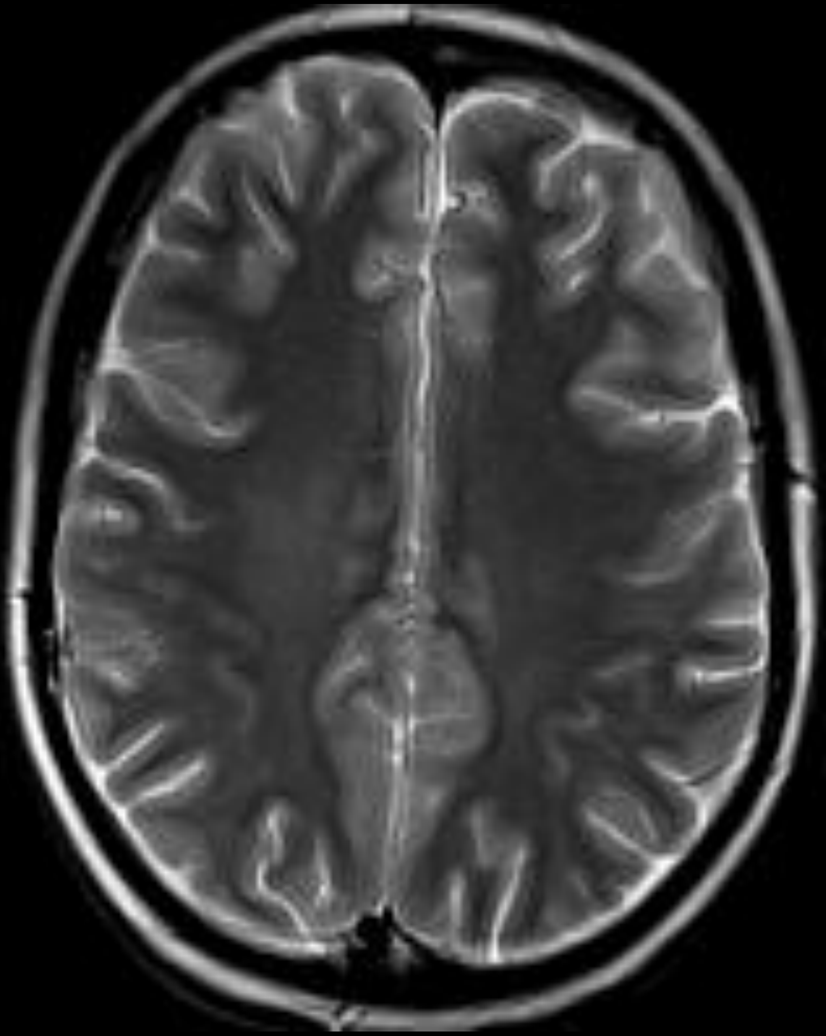
acute MTX-toxicity

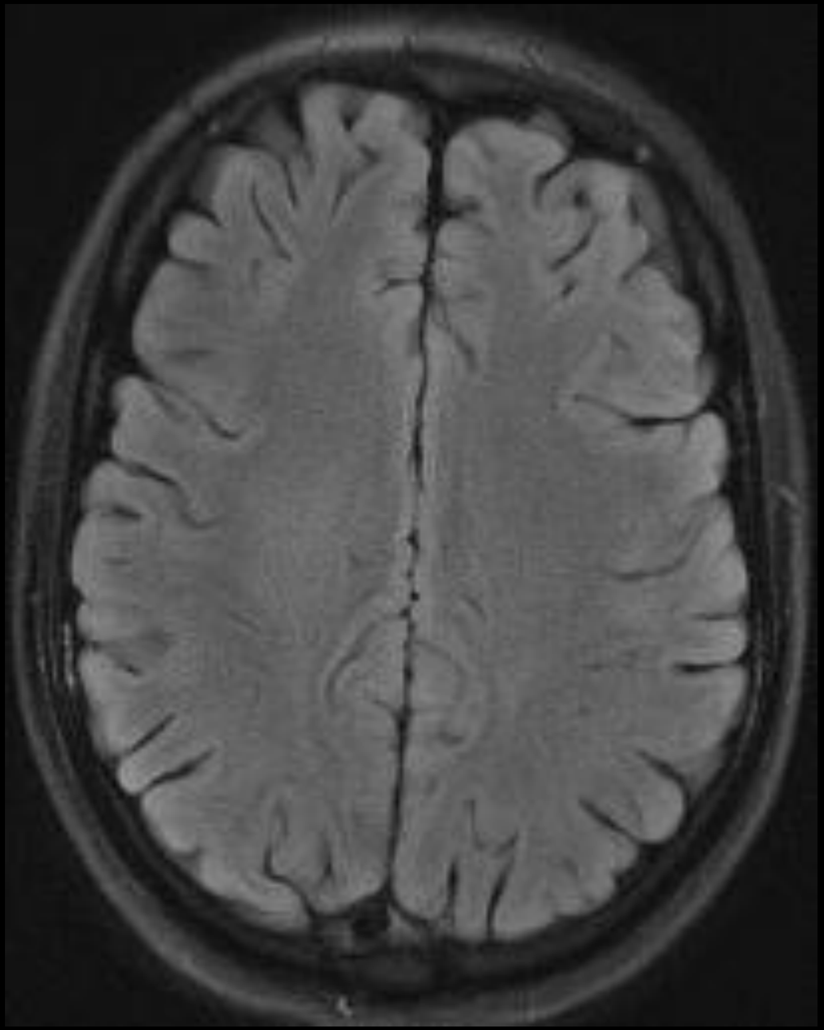
- restricted diffusion is diagnostic
- reversible
- strokelike event
- 6-11 d nach MTX (intrathecal)

Rollins et al. AJNR 2004

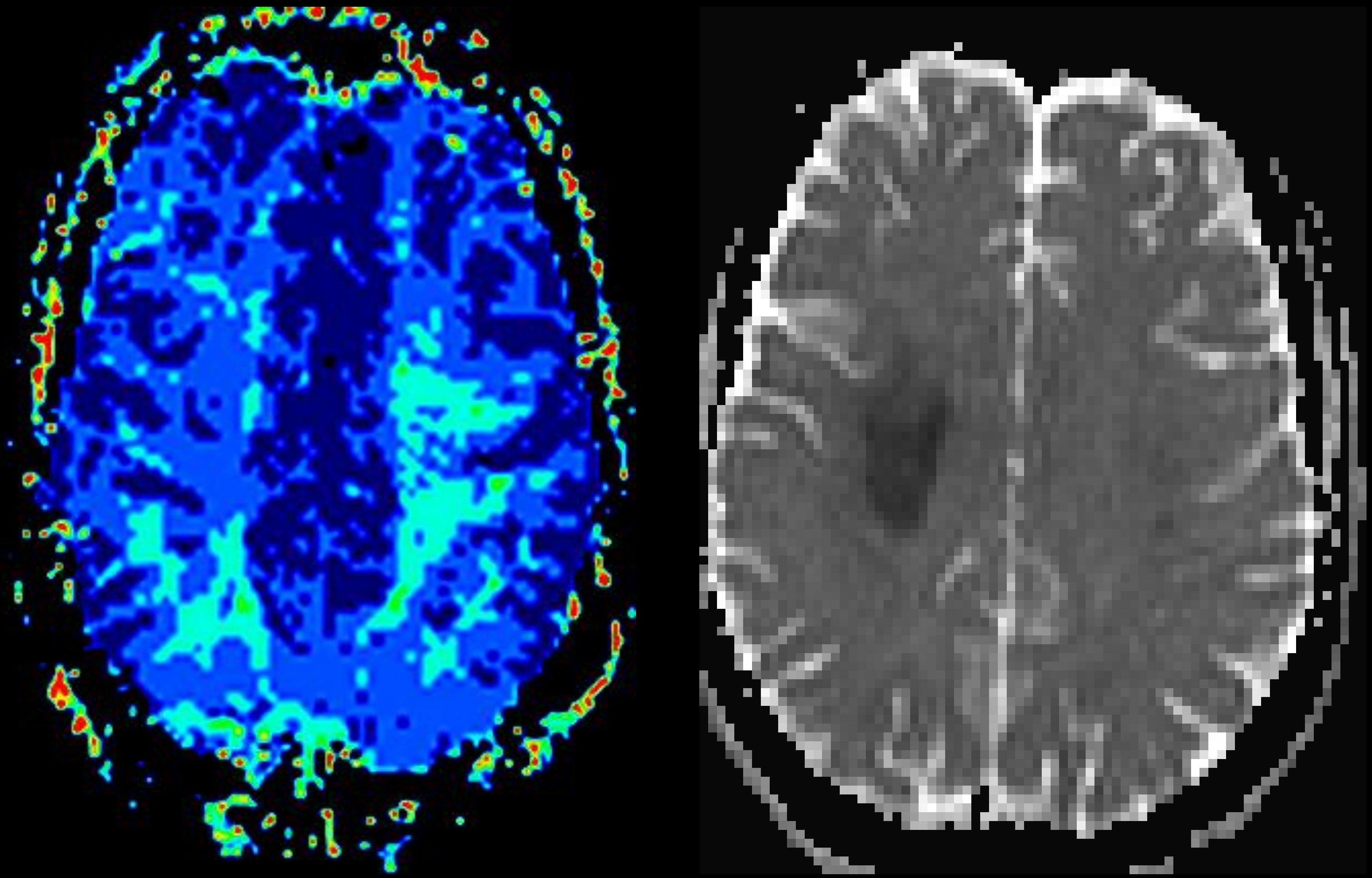


acute MTX-leukoencephalopathy

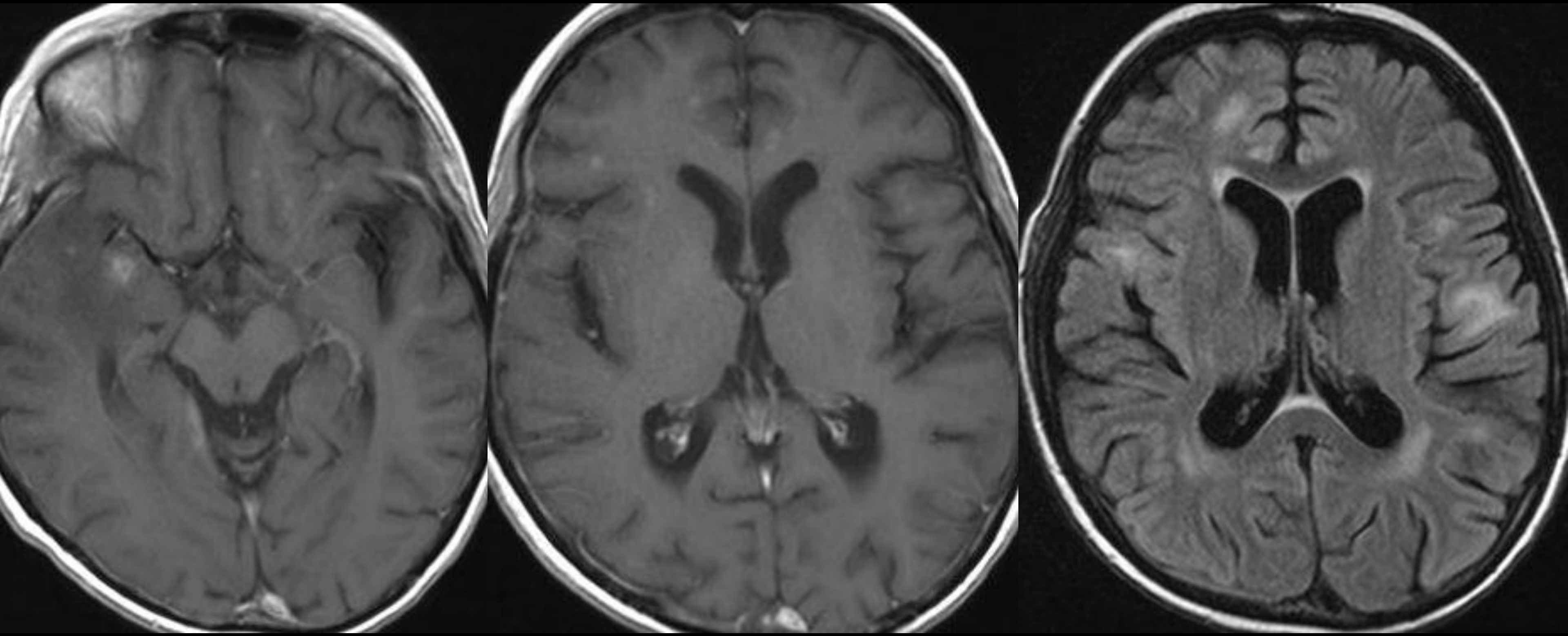




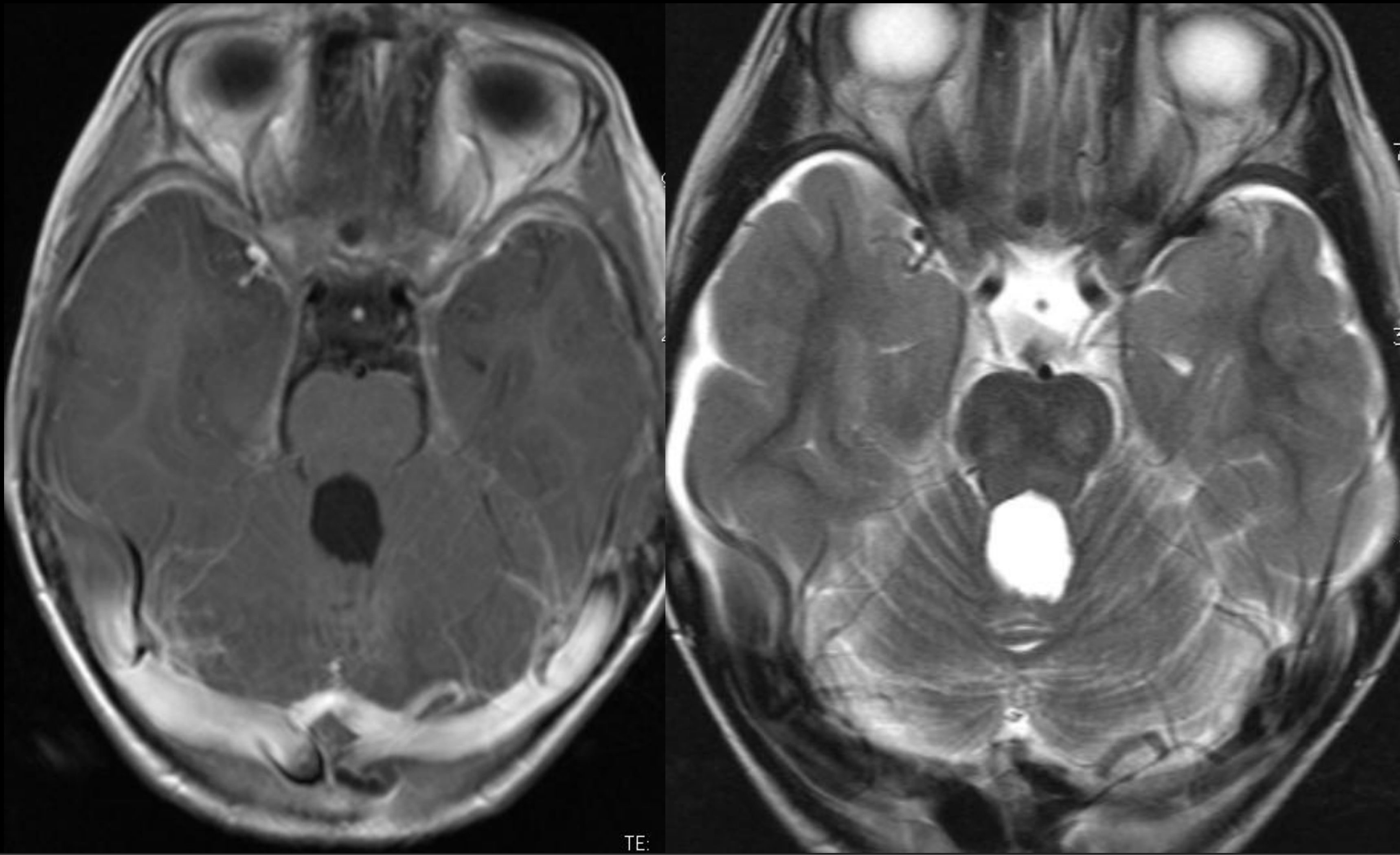
acute MTX-leukoencephalopathy



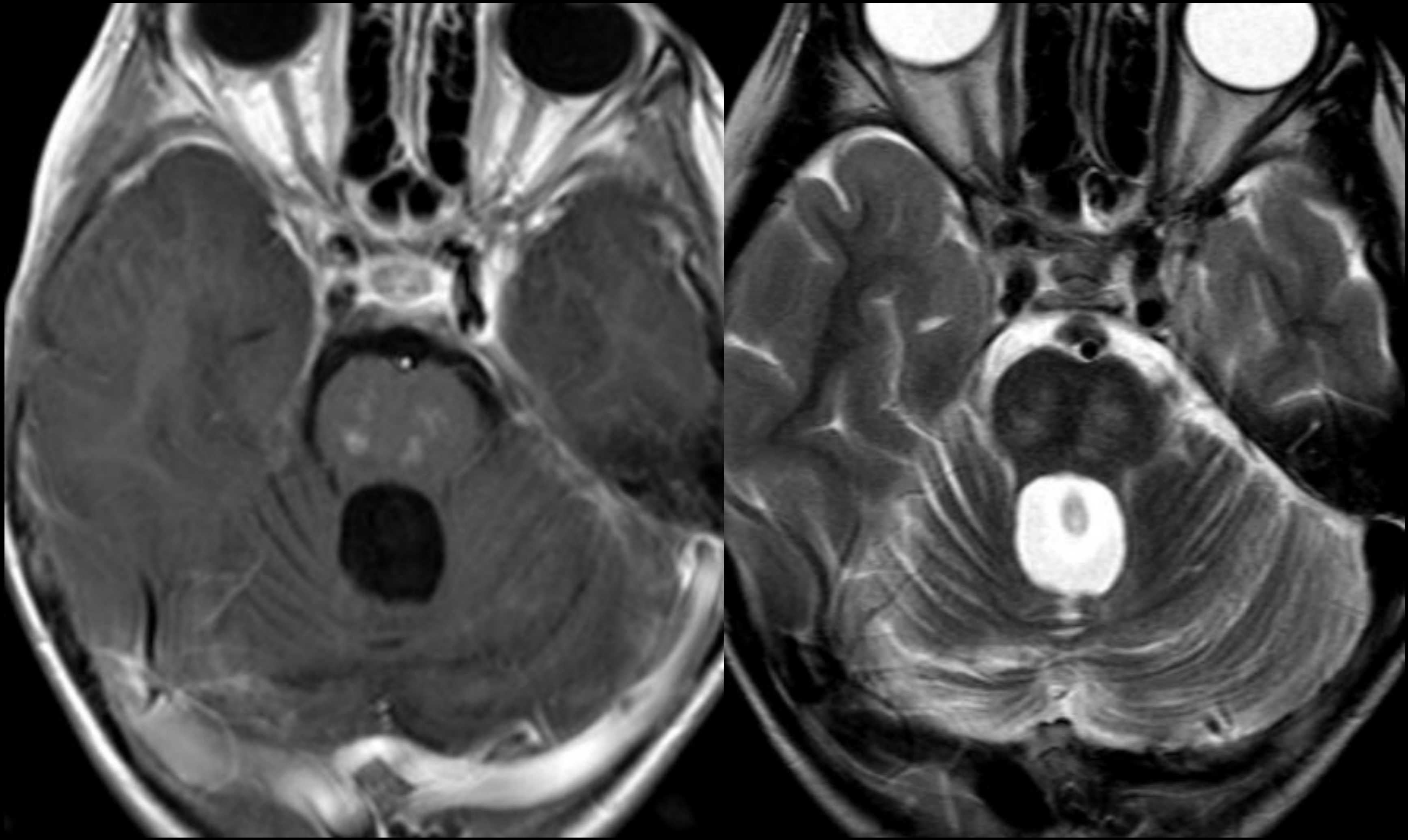
necrotising LEP (MTX after irrad.)



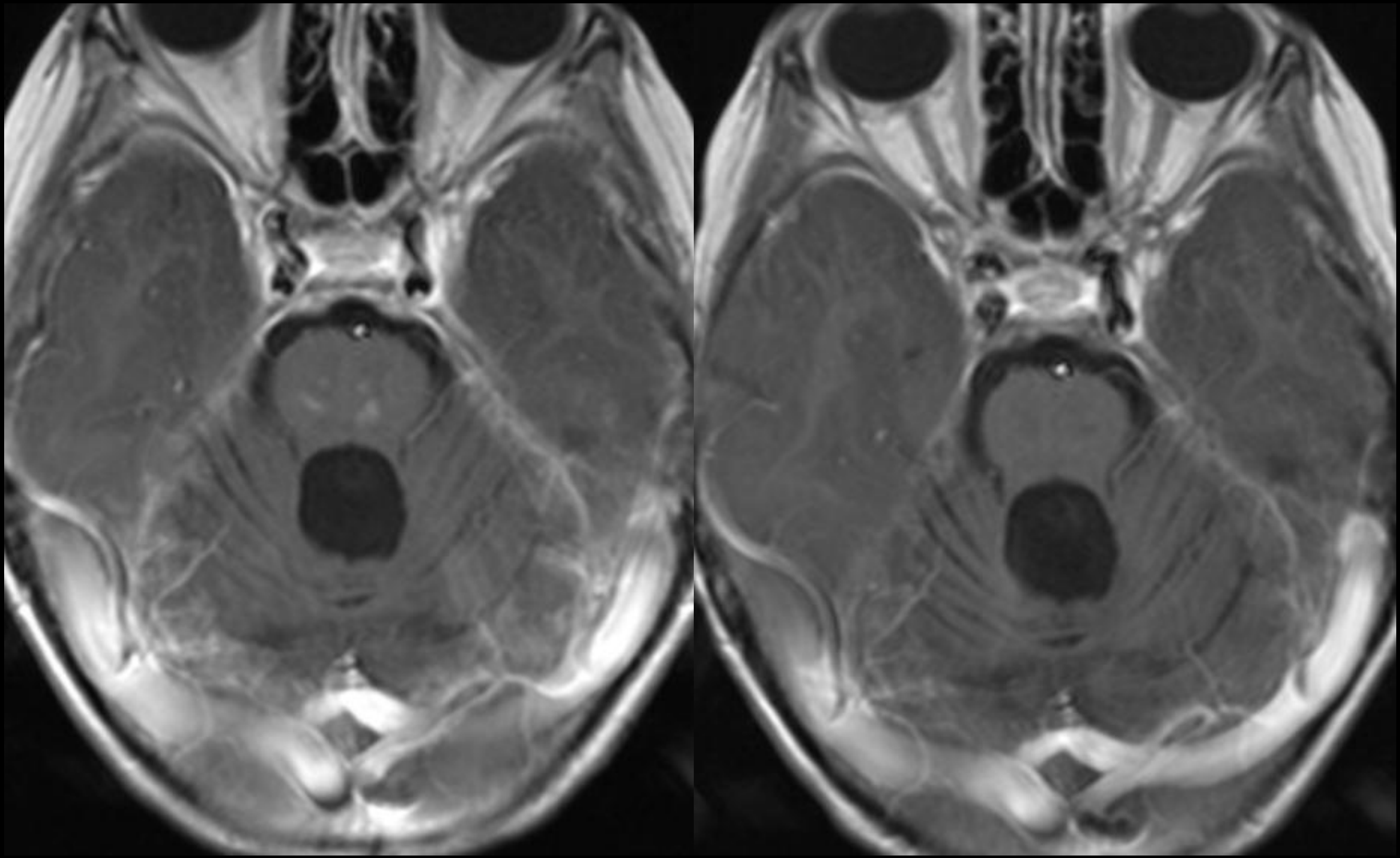
MB 3 months after irradiation



MB 6 months after irradiation



MB 9 and 12 months after irradiation



simple rule

- MB (and probably other embryonal tumors) and ependymomas recur not in another place within the brain parenchyma but either as local recurrence and/or meningeal dissemination

Warmuth-Metz et al: Neuro Oncol 2011

therefore

- a new lesion within the brain at another place can only be treatment related (radiation reaction or second tumor even if histology is eg PNET)

nomenclature of a radiation reaction

- immediate reaction:
  edema during irradiation
- early delayed reaction:
  weeks to months after termination of irradiation
- late delayed reaction:
  3 months or later (up to many years) nach treatment, usually within 2 years
  Rabin BM et al: Radiation induced changes in the CNS Radiographics 1996

time course of temporary radiation reaction

- typical development of WML after a median of 7.8 months after the start of irradiation (1.9-13 months)
- reduction after a median of 6.2 months (1.7-23.5 months)

Fouladi M et al: J Clin Oncol 2004; 22: 4551

- T2-lesions and contrast enhancement after an average of 6 months after IMRT (4-9 months)
- reduction within 6 months (3-25 months)

Muscal JA et al: Int J Radiation Oncol Biol Phys (2009) 73: 214

suspicion of a radiation reaction after accelerated irradiation and carboplatin

- incidence 13.5%
- enhancement within or surrounding a previously non-enhancing tumor
- enhancement with a distance to the tumor but within the treatment field
- enhancement in the periventricular white matter especially caplike around the ventricular borders or enhancement in the corpus callosum
- soap bubble- or swiss cheese pattern of enhancement

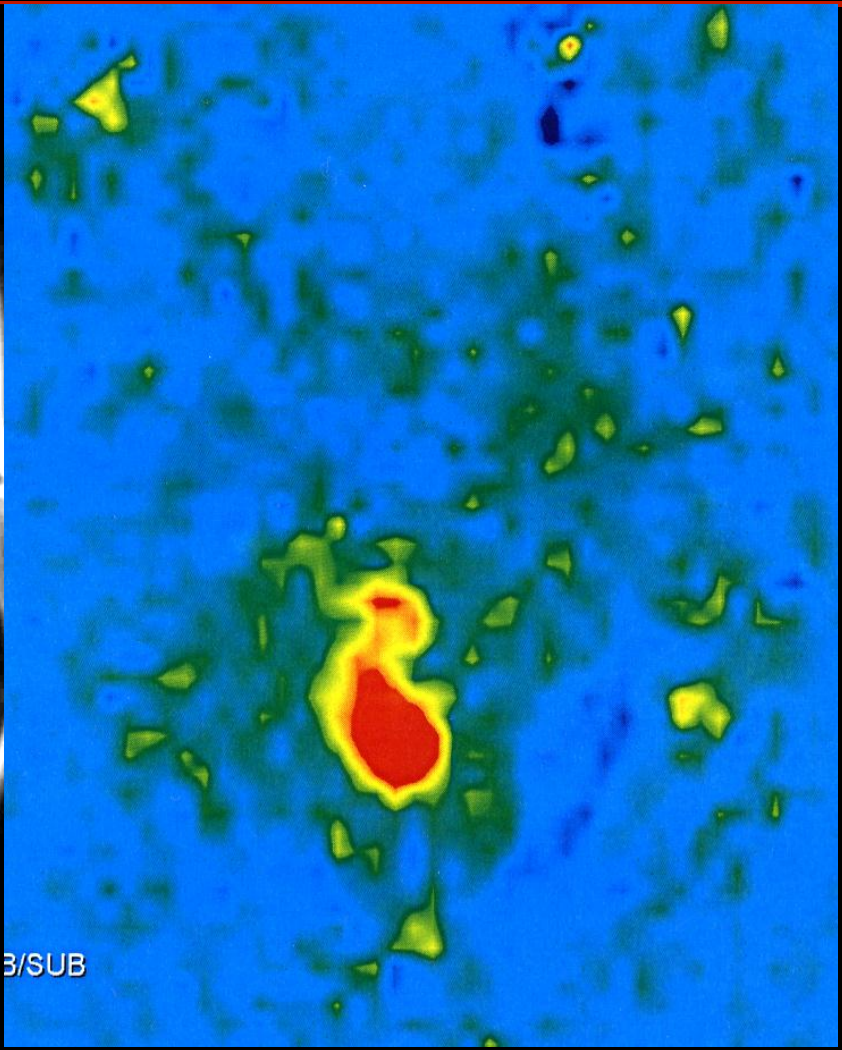
Kumar A J et al. Radiology 2000;217:377-384

suspicion of radiation necrosis

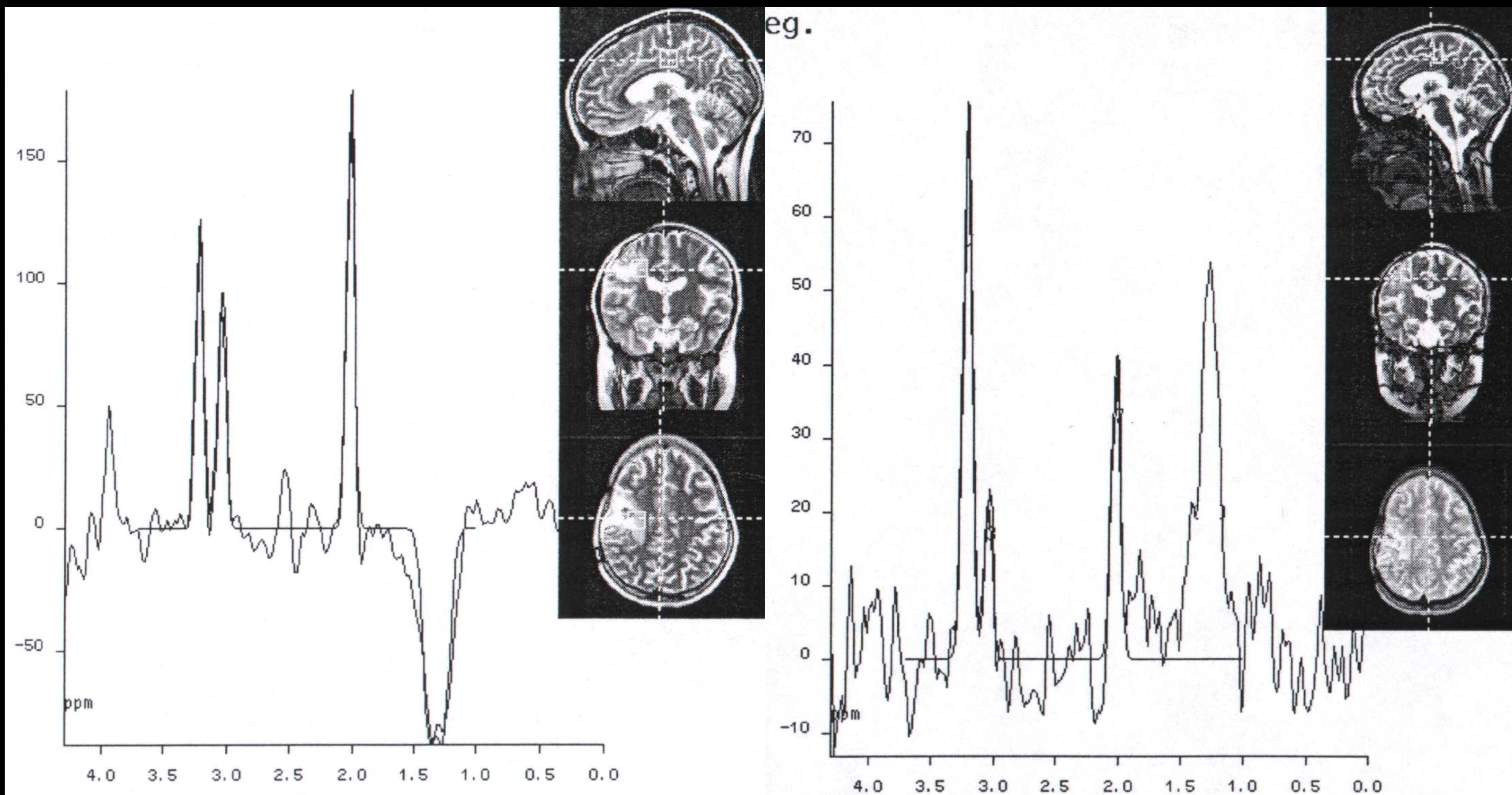
- enhancement
  - cortical enhancement 61%
  - only cortical enhancement 2%
  - white matter 98%
  - only white matter 39%
- enhancement in corpus callosum 27%
- spreading wave front 98% (vs. nod.)
- swiss cheese/soap bubble 90% (vs. solid)
- n=52

Rogers et al: J Neurooncol 2011; 101

perfusion imaging



MRS


eg.
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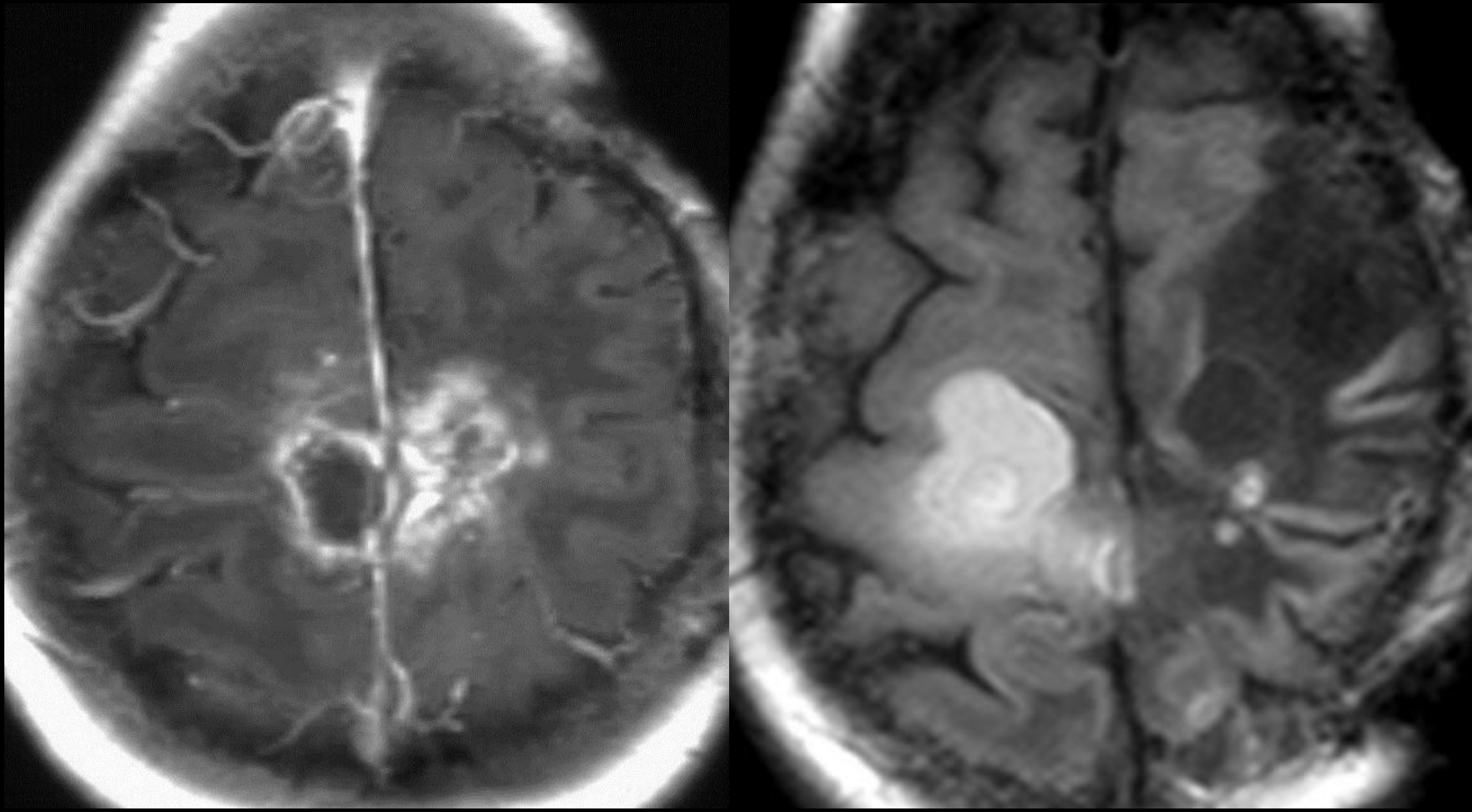
chronic radiation necrosis

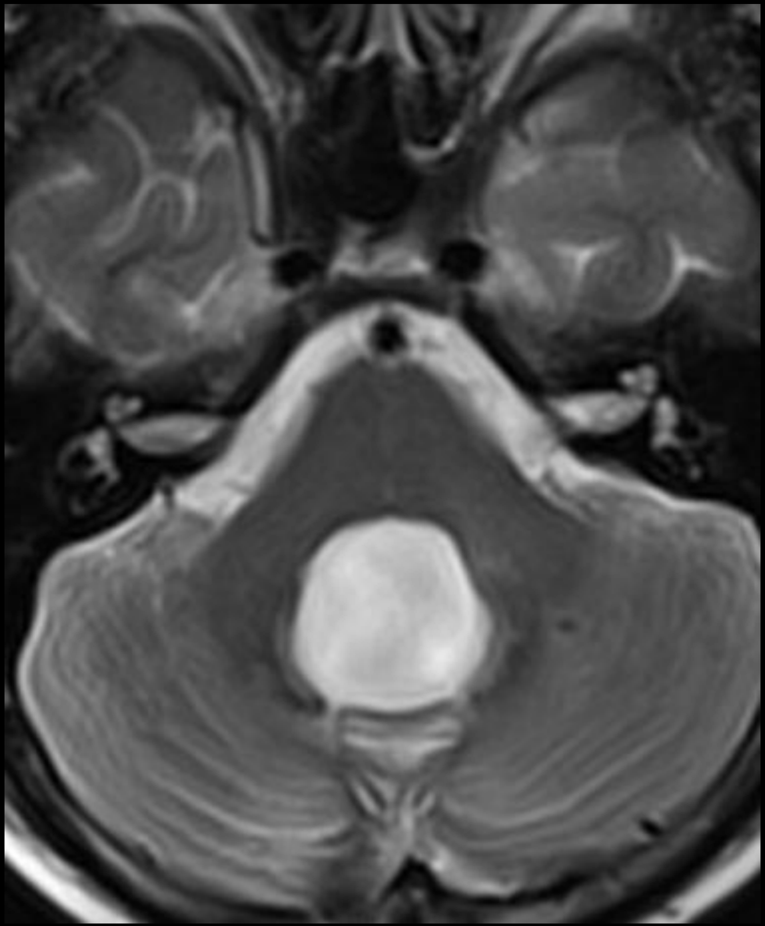


cavernous hemangioma

- after irradiation in children
  - after 1-26 years (mean 5-16 y)
  - 3.4% incidence after irradiation at age 7y?
  - possible precursor capillary teleangiectasie
  - dose >30 Gy, dose related
  - risk of bleeds higher than in inborn cavernomas
  - no true incidence, as the demonstration is dependant on the MR-sequences used and has not been systematically evaluated

Burn et al.: J Neurosurg 2007
Jain et al: AJNR 2005

cavernous hemangioma



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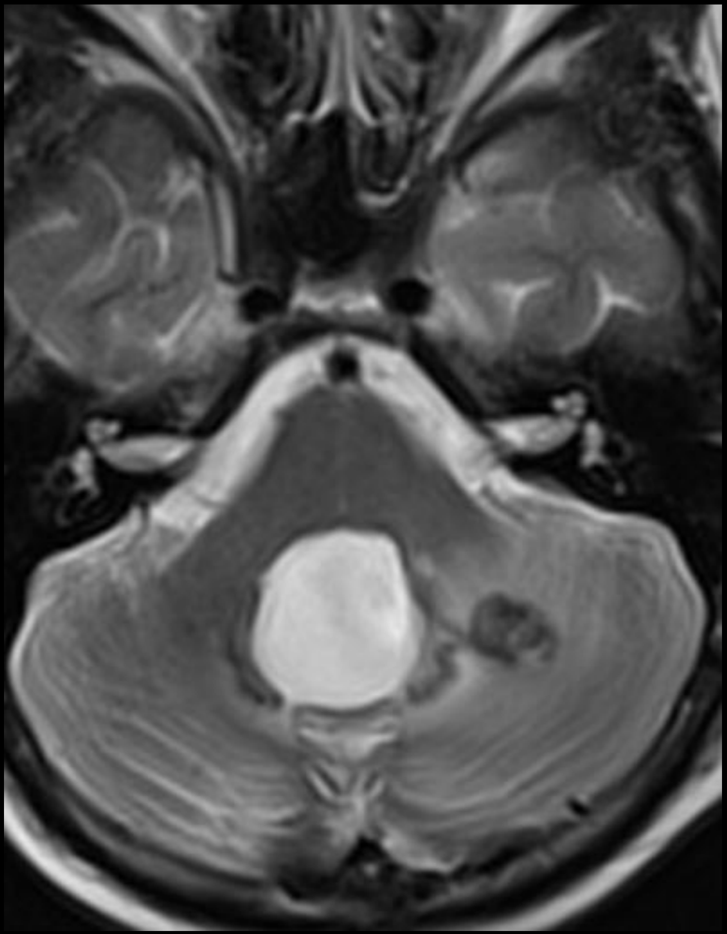

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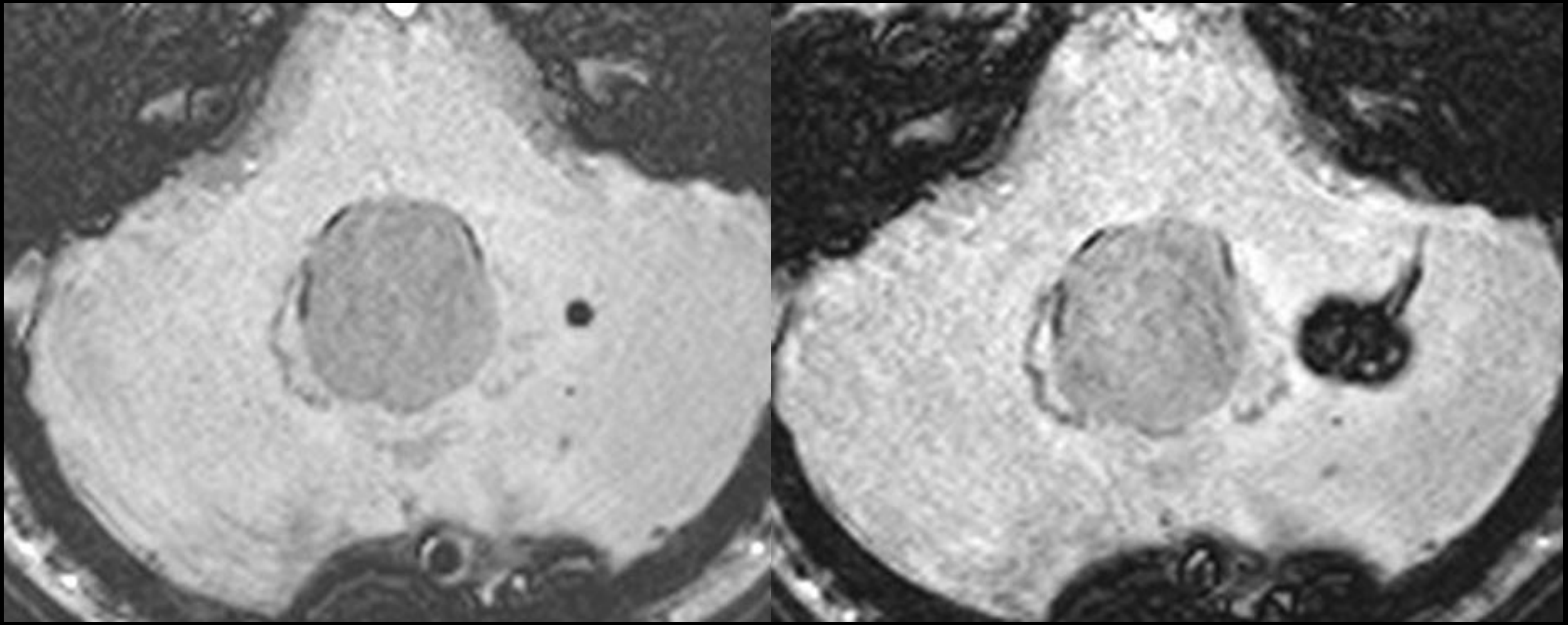
cavernous hemangioma



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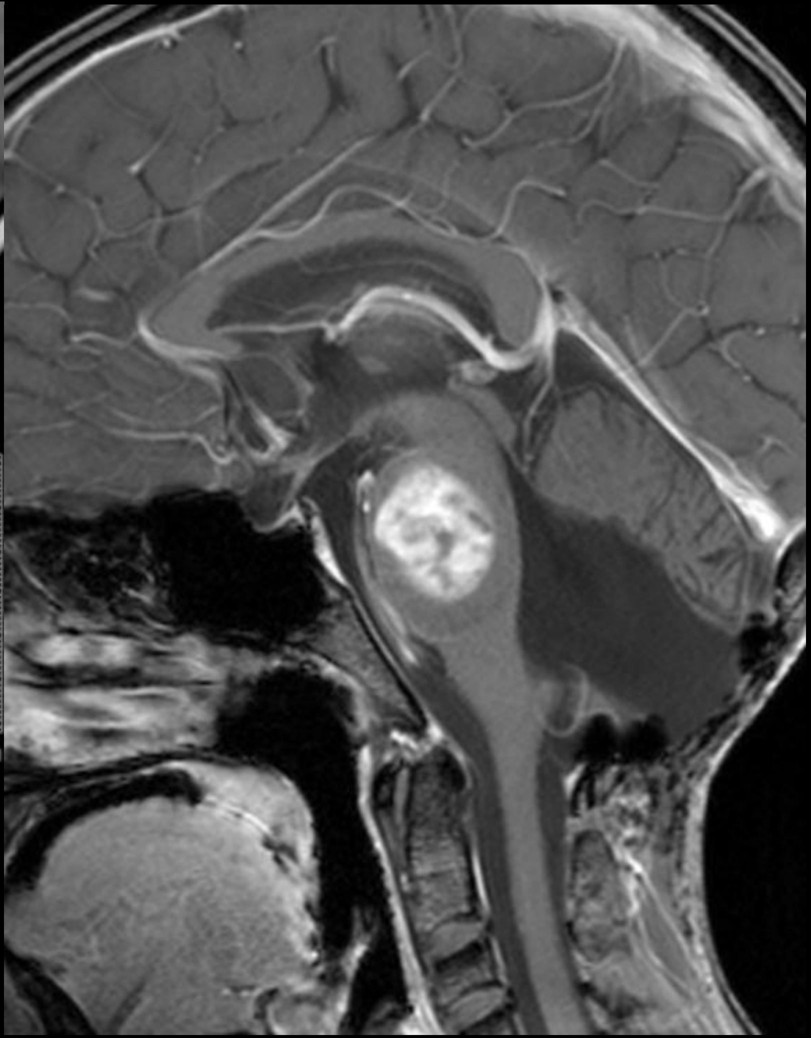
secondary tumors

- main cause irradiation
  - meningiomas, often high grades
  - typical interval 10 y and more

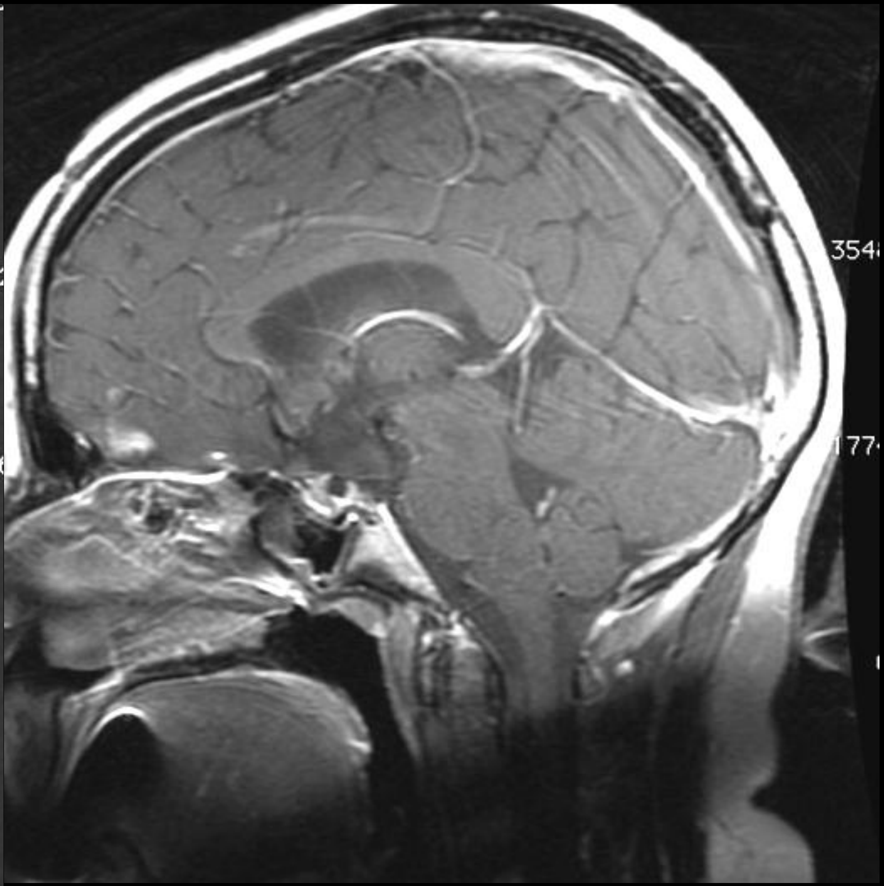
Müller H et al. Strahlenther Onkol 2012

- combined treatment
  - meningiomas, high grade gliomas, PNETs
  - typical intervall 9 y
- only after chemotherapy?
- extremely bad prognosis

secondary tumors



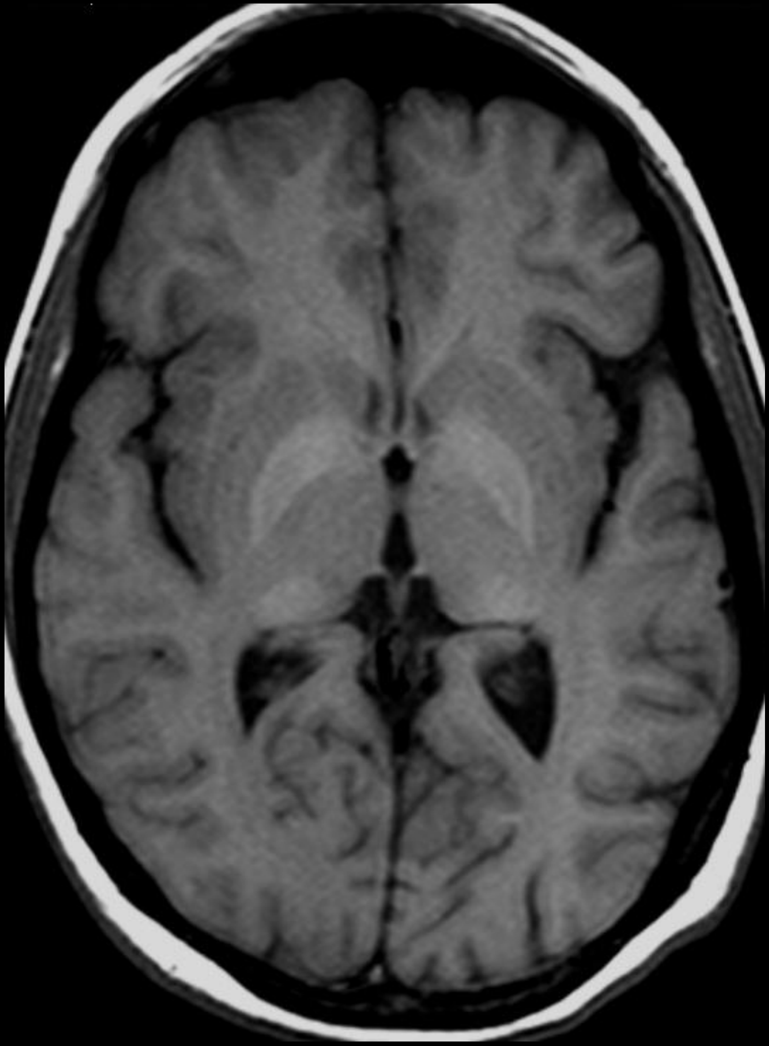
hypothalamic obesity



Müller H, Warmuth-Metz et al.:
Eur J Endocrin 2011; 165: 17-24

3/2010 LGG 8/2010

T1-signal of nuclei



bright T1 in nuclei

- myelindegradation? myelinrepair (NF1)
- treatmentconsequence? dent. nucl. after irradiation Kasahara S et al: Radiology 2011; 258
- storage of Gadolinium
  - linear vs. cyclic Gd-chelates
  - patients with normal renal function!
  - correlation to the amount of Gadolinium

Kanda T et al: Radiology 2015;epub
Errante Y et al: Invest Radiol 2014; 49
Radbruch A et al: Radiology 2015; 275

Danke - thank you