



## Imaging of brain tumours and metastases

Professor Marco Essig, MD; Lars Gerigk

**Magnetic resonance imaging is the most sensitive method for diagnosing brain tumours. Modern protocols allow further insights into their pathophysiology.**

**T**he goals and requirements for brain tumour imaging are complex and involve making a differential diagnosis subsequently resulting in a diagnosis, while accurate lesion grading is needed in the case of tumour description. Imaging is also involved in the decision-making process for therapy and precise planning of surgical or radiotherapeutic interventions. Neuroimaging techniques are also essential for monitoring of (residual) disease and possible therapy related side effects.

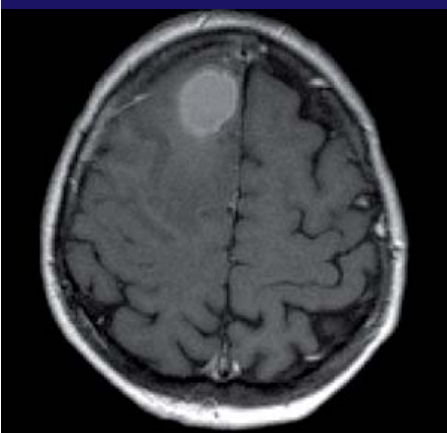
Due to the high tissue contrast and the non-invasive nature of the method, magnetic resonance imaging (MRI) is accepted as the most sensitive method for diagnosing brain tumours [1]. The exclusion of a possible brain tumour is one of the most common indications for neuroimaging using MRI.

The classification of brain tumours is still controversial, and includes classification by location or histology. The most common classification is that of the World Health Organization (WHO) summarised in the so-called 'Blue Book' [2]. Brain tumours are categorised into primary versus secondary tumours, based on the tissue of origin, and intra-axial versus extra-axial tumours based on the origin of growth [3]. The most common primary intra-axial tumours are neuroepithelial tumours including astrocytomas, oligodendrogliomas, mixed gliomas and other more rare neuronal-glioma tumours with the glioblastoma multiforme as the most common brain tumour [4]. Meningiomas are the most common primary extraaxial tumours [5] and account for about 20% of all brain tumours. In adults, however, secondary, metastatic brain lesions far

outnumber primary tumours with a high incidence in systemic cancers such as lung and breast [6].

The MRI protocol to assess brain tumours includes unenhanced T1-, T2- and FLAIR-weighted sequences followed by contrast studies in T1 weighting. The unenhanced T1-weighted sequences are used to rule out intraleSIONAL bleeding or visualisation of e.g. melanin, which is frequently found in metastases of melanoma (see Figure 1).

**Figure 1: Haemorrhage in a melanoma metastases**



T1 Spin-Echo imaging presents high signal of the lesion, indicating the presence of methaemoglobin.

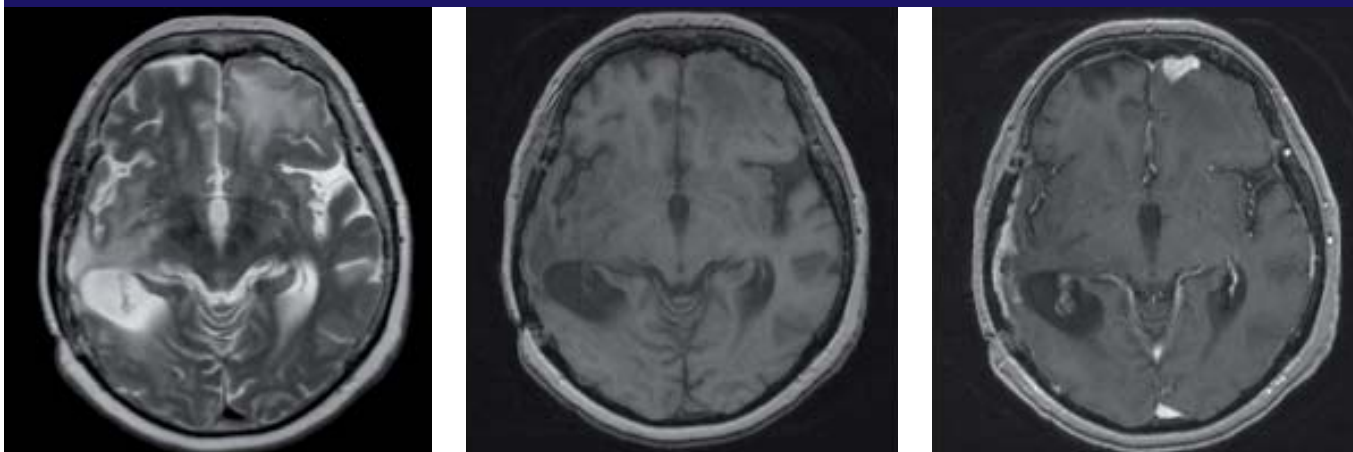
T2-weighted Fast SE sequences and FLAIR is used to display the margins of a tumour and its surrounding oedema [7, 8]. In uncooperative patients a motion insensitive acquisition should be used [9]. Contrast enhancement studies are mandatory in the assessment of patients with cerebral tumours. The standard dose employed for MRI of the CNS is 0.1 mmol/kg body weight although numerous studies have shown that lesion

detection may be improved with the use of higher doses and dedicated sequences [10, 11]. Contrast enhanced MRI helps in distinguishing tumours from other pathologic processes, and is better to depict signs of tumour response to therapy, such as change in size, morphology and degree of contrast material enhancement (see Figure 2). The sequences after contrast media should at least include two planes of T1-weighted sequences, and, if possible, a volumetric sequence, e.g. 3D T1-weighted imaging to allow for reconstruction in different planes and volumetric assessment of the lesions.

Due to the presence of the Blood-Brain-Barrier (BBB) the current available MR contrast media do not leak into the brain tissue [12]. Substances with a molecular weight higher than 180 daltons (Da), which include all available imaging contrast media, generally cannot cross the BBB. In intraaxial primary tumours, mainly gliomas, the BBB can be compromised by neovascularisation and direct damage due to tumour ingrowth. In secondary, metastatic intraaxial tumours and extraaxial tumours the vessels are different from normal cerebral vasculature and have no or strongly disturbed BBB [13,14]. Those entities normally have a strong enhancement pattern presenting the whole tumour as enhancing mass.

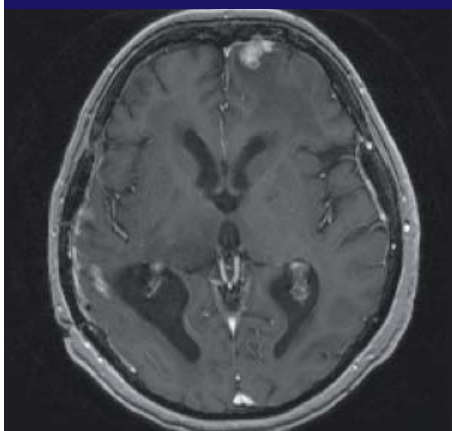
Contrasting material enhanced MRI is the accepted standard of reference for assessment of the integrity of the blood-brain barrier. Compared with contrast-enhanced computed tomography, MRI with gadolinium-based contrast agents is far more sensitive and depicts even subtle disruptions of the BBB that are caused by a variety of noxious agents, neoplastic or inflammatory processes, or ischaemic stress [15].

**Figure 2 a-c: MRI of a patient with frontal enhancing tumor (Meningeoma)**



T2 shows oedema in the frontal and temporal lobe with no circumscribed tumorous lesion. After contrast media application (0.1 mmol of gadobutrol, Gadovist, Bayer Healthcare) the lesion in the frontal lobe is well circumscribed and could be demarcated from the oedema. Note also the enhancement of the meninges in the temporo-parietal region.

**Figure 2d: Using a standard contrast media (Dotarem, Guerbet)**



Using a standard contrast media (Dotarem, Guerbet) the enhancement is less pronounced and the meningeal enhancement not as obvious. This intraindividual comparative study shows the importance of the use of high quality contrast media for the patient safety and security of diagnosis.

The use of gadolinium contrast media is therefore standard in the assessment of cerebral tumours (see Figure 2).

In the past few years a number of advanced, non enhanced and contrast enhanced MRI techniques have been developed that provide new insights into the pathophysiology of brain tumours, mainly gliomas. These techniques include MR-spectroscopy (MRS), perfusion MRI [16], dynamic contrast enhanced (DCE) MRI [16] and diffusion tensor MR. The contrast perfusion MRI

technique is now recognised as an important new means for assessing tumour grading and follow up of various treatment strategies (see Figure 3). Another of these techniques, dynamic contrast enhanced MRI, is also gaining acceptance for the same purposes. Perfusion-weighted imaging (PWI) in brain tumours has benefits for three major fields: differential diagnosis, biopsy planning, and treatment monitoring. The basic principle of PWI using dynamic susceptibility-weighted contrast-enhanced MRI is as follows: The first-pass of a contrast bolus, e.g. 0.1 mmol of Gadovist, in brain tissue is monitored by a series of T2\*-weighted MR images. The susceptibility effect of the paramagnetic contrast agent leads to a signal loss that can be converted, using the principles of the indicator dilution theory, into an increase of the contrast agent concentration. From these data, parameter maps of cerebral blood volume (CBV) and cerebral blood flow (CBF) can be derived. Regional CBF and CBV values can be obtained by region-of-interest analysis. Our experience of brain tumour differentiation is that PWI has superior diagnostic performance in predicting glioma grade and in differentiating glioblastoma from other tumour entities (metastases, meningiomas, and CNS-lymphomas) when compared to spectroscopic imaging and dynamic contrast-enhanced MRI [16]. Correct grading of gliomas has

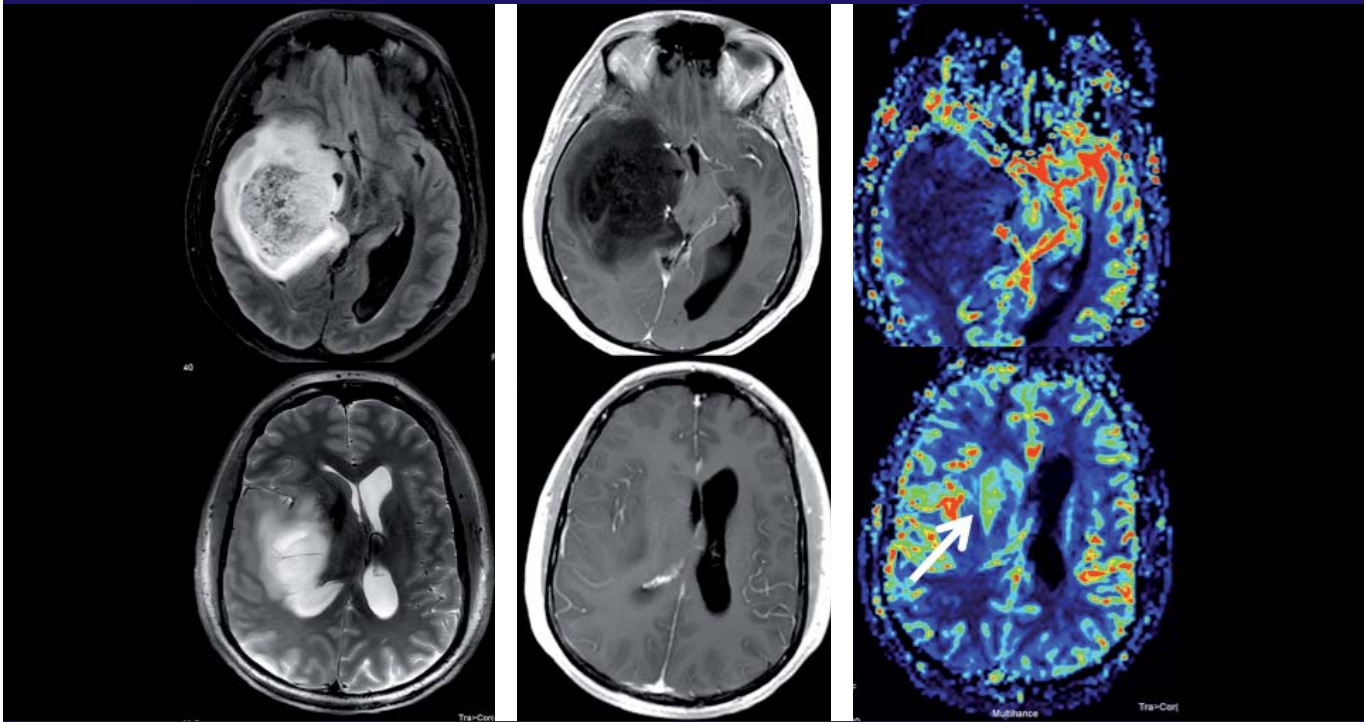
significant clinical impact, because adjuvant therapy after surgery is usually administered to high-grade but not low-grade gliomas.

Perfusion-weighted imaging can easily be incorporated as part of the routine clinical evaluation of intracranial mass lesions due to the relatively short imaging and data processing times and the use of a standard dose of contrast agent. Thus, PWI together with conventional MRI should be regarded as the test of choice to diagnose and monitor brain tumours before, during, and after therapy.

## Conclusion

The use of contrast media is essential in MRI for the diagnostic work-up of patients with cerebral tumours. The hospital pharmacist should have a basic understanding about the availability of different contrast media with different properties and potential. The contrast in the final images is influenced by the dosage of the contrast agent, the used MR field strength and the application strategy. In modern neuroimaging protocols, however, functional contrast enhanced techniques such as PWI, MRS and DCE allow further insights into the pathophysiology of cerebral tumours and provide information that complements the superb morphological assessment with standard imaging techniques.

**Figure 3: Large glioma in a 34-year-old patient**



T2 (A-B) presents a large heterogenous tumour in the right temporo-parietal and frontal region. T1 GRE after contrast media (0.1 mmol/kg of Gadobutrol) (C-D) did not show any contrast enhancement within the tumour. Perfusion MRI – CBF maps (E-F) present a low perfused caudal part of the tumour indicating a low grade lesion, but with an increased perfusion in the upper frontal area of the tumour (arrow) indicating a high grade (WHO III) lesion.

## Author for correspondence

Professor Dr med Marco Essig  
Department of Radiology, DKFZ  
280 Im Neuenheimer Feld  
D-69120 Heidelberg, Germany  
m.essig@dkfz.de

## Co-author

Lars Gerigk

## References

- Levin VA, Leibel SA, Gutin PH. Neoplasms of the central nervous system. In: DeVita VT Jr, Hellman S, Rosenberg SA, editors. *Cancer: Principles and Practice of Oncology*. 6th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2001;2100-60.
- World Health Organization. *Classification of Tumours of the Central Nervous System*. Zürich. WHO, 4th edition, June 2007.
- Cenacchi G, Giangaspero F. Emerging tumor entities and variants of CNS neoplasms. *J Neuropathol Exp Neurol*. 2004; 63:185-92.
- Kleihues P, Ohgaki H. Primary and secondary glioblastomas: from concept to clinical diagnosis. *Neuro Oncol*. 2001;52:181-8.
- Longstretz WE, Dennis LK, McGuire VM, et al. Epidemiology of intracranial meningioma. *Cancer*. 1993;72:639-48.
- Patchell RA. Brain metastases. *Neurol Clin*. 1991;9:817-27.
- Essig M, Hawighorst H, Schoenberg SO, et al. Fast fluid-attenuated inversion-recovery (FLAIR) MR imaging in the assessment of intraaxial brain tumors. *J Magn Reson Imag*. 1998;8:789-98.
- Essig M, Schoenberg SO, Hawighorst H, et al. Cerebral gliomas and metastases: Assessment with contrast enhanced fast fluid-attenuated inversion-recovery MR imaging. *Radiology*. 1999;210:551-7.
- Wintersperger BJ, Runge VM, Biswas J, et al. Brain magnetic resonance imaging at 3 Tesla using BLADE compared with standard rectilinear data sampling. *Invest Radiol*. 2006;41:586-92.
- Erickson BJ, Campeau NG, Schreiner SA, Buckner JC, O'Neill BP, O'Fallon JR. Triple-dose contrast/magnetization transfer suppressed imaging of 'non-enhancing' brain gliomas. *J Neurooncol*. 2002;60:25-9.
- Giesel FL, Mehndratta A, Risse F, Rius M, Zechmann CM, et al. Intraindividual comparison between gadopentate and gadobutrol for magnetic resonance perfusion in normal brain and intracranial tumors at 3T. *Acta Radiol*. 2009;43:843-53.
- Essig M, Weber MA, von Tengg-Kobligh H, Knopp MV, Yuh WT, Giesel FL. Contrast-enhanced Magnetic Resonance Imaging of Central Nervous Tumors: Agents, Mechanisms and Applications. *Top Magn Reson Imaging*. 2006;17:89-106.
- Fidler IJ, Yano S, Zhang RD, et al. The seed and soil hypothesis: vascularisation and brain metastases. *Lancet Oncol*. 2002;3(1): 53-7.
- Groothuis DR. The blood-brain and blood-tumor barriers: a review of strategies for increasing drug delivery. *Neuro Oncol*. 2000;2(1):45-59.
- Runge VM. A review of contrast media research in 1999-2000. *Invest Radiol*. 2001; 36(2): 123-30.
- Essig M, Giesel F, Stieltjes B, Weber MA. Functional imaging of brain tumors (perfusion, DTI and MR spectroscopy). *Radiologe*. 2007;47:513-9.