Diffusion-Weighted MR Imaging in Brain Tumor

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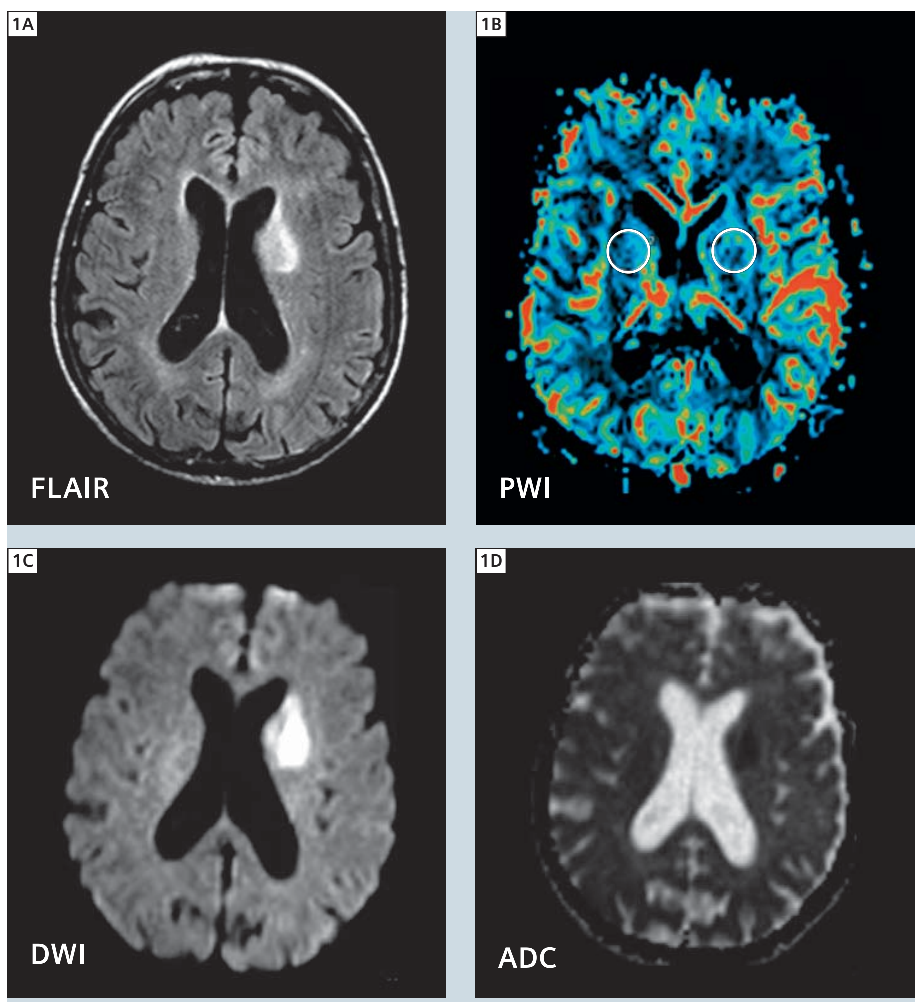
Introduction

Primary neoplasms of the central nervous system (CNS) have a prevalence of between 15,000 and 17,000 new cases annually in the United States and are estimated to cause the deaths of 13,000 patients. Gliomas are the leading cause of primary CNS tumors, accounting for 40–50% of cases and 2–3% of all cancers[4]. Despite new treatment techniques, patients' survival still remains very low, varying between 16 and 53 weeks.
It is generally accepted that conventional magnetic resonance imaging (MRI) tends to underestimate the extent of the tumor, which can in turn lead to a suboptimal treatment. New functional magnetic resonance imaging sequences, such as diffusion tensor imaging (DTI) and diffusion-weighted imaging (DWI), have been widely used to evaluate such tumors.

Diffusion-weighted MR image

Diffusion-weighted imaging is based on the random or Brownian motion of water molecules in relation to their thermal energy.
DWI has been used to assess brain tumors and while it has had limited success as a definitive prognostic tool, its proponents suggest that in certain settings it can increase both the sensitivity and specificity of MR imaging.
One example of a specific arena in which DWI may be helpful is in distinguishing between brain abscesses and necrotic and cystic neoplasms on MRI. This differentiation is still a challenge on both clinical and radiological setting. The abscesses have a high signal on DWI and a reduced Apparent Diffusion Coefficient (ADC) within the cavity. This restricted diffusion is thought to be related to the characteristic of the pus in the cavity; this may in turn lead to reduced water mobility, lower ADC, and bright signal on DWI. By contrast, necrotic and cystic tumors display a low signal on DWI (similar to the CSF in the ventricles) with an increased ADC as well as isointense or hypointense DWI signal intensity in the lesion margins.

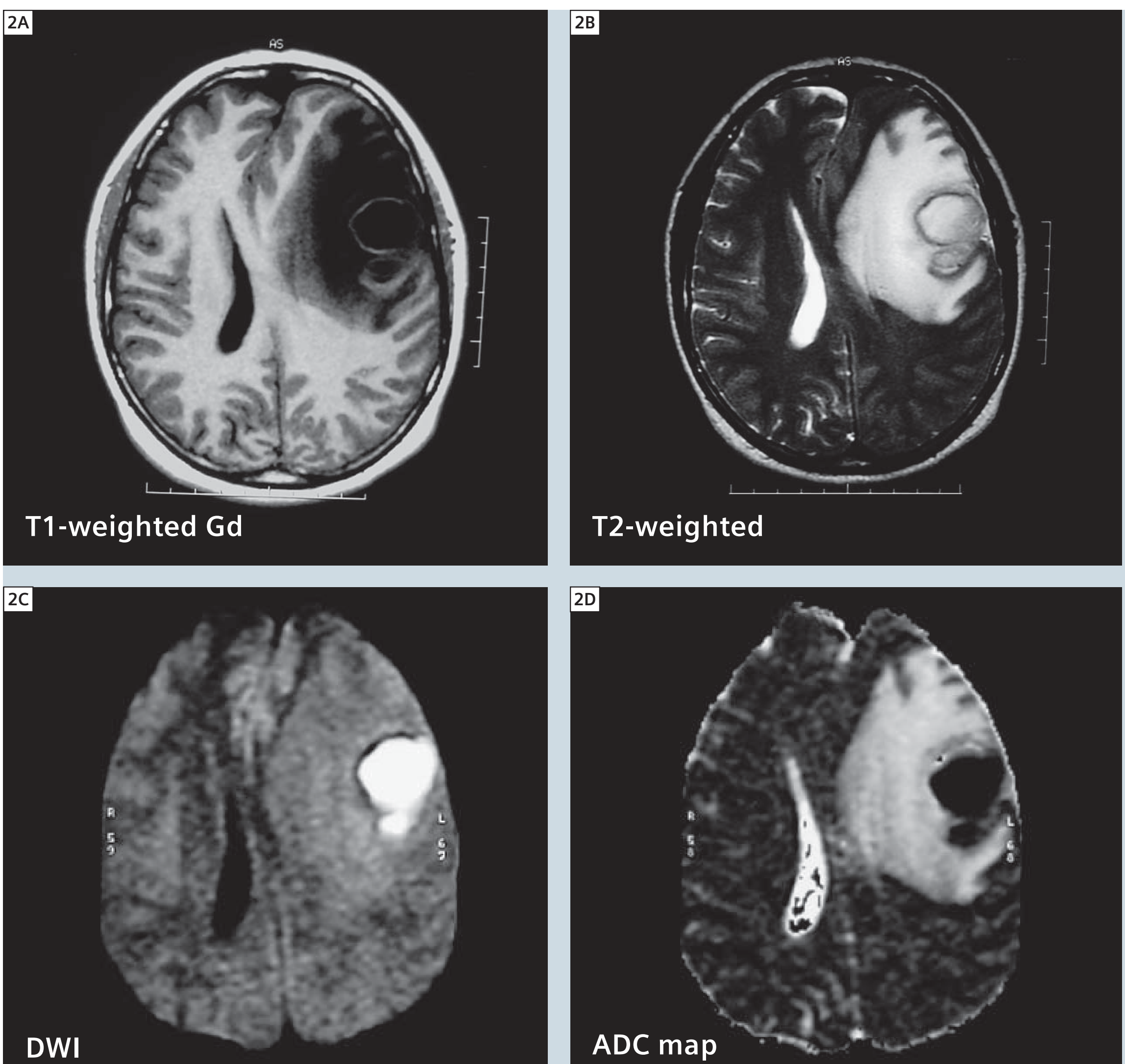


1 72-year-old female presented with mental and language disturbance, since 20 days. Enhancing lesion, low perfusion, restricted diffusion on DWI and ADC.
Diagnosis: Lymphoma

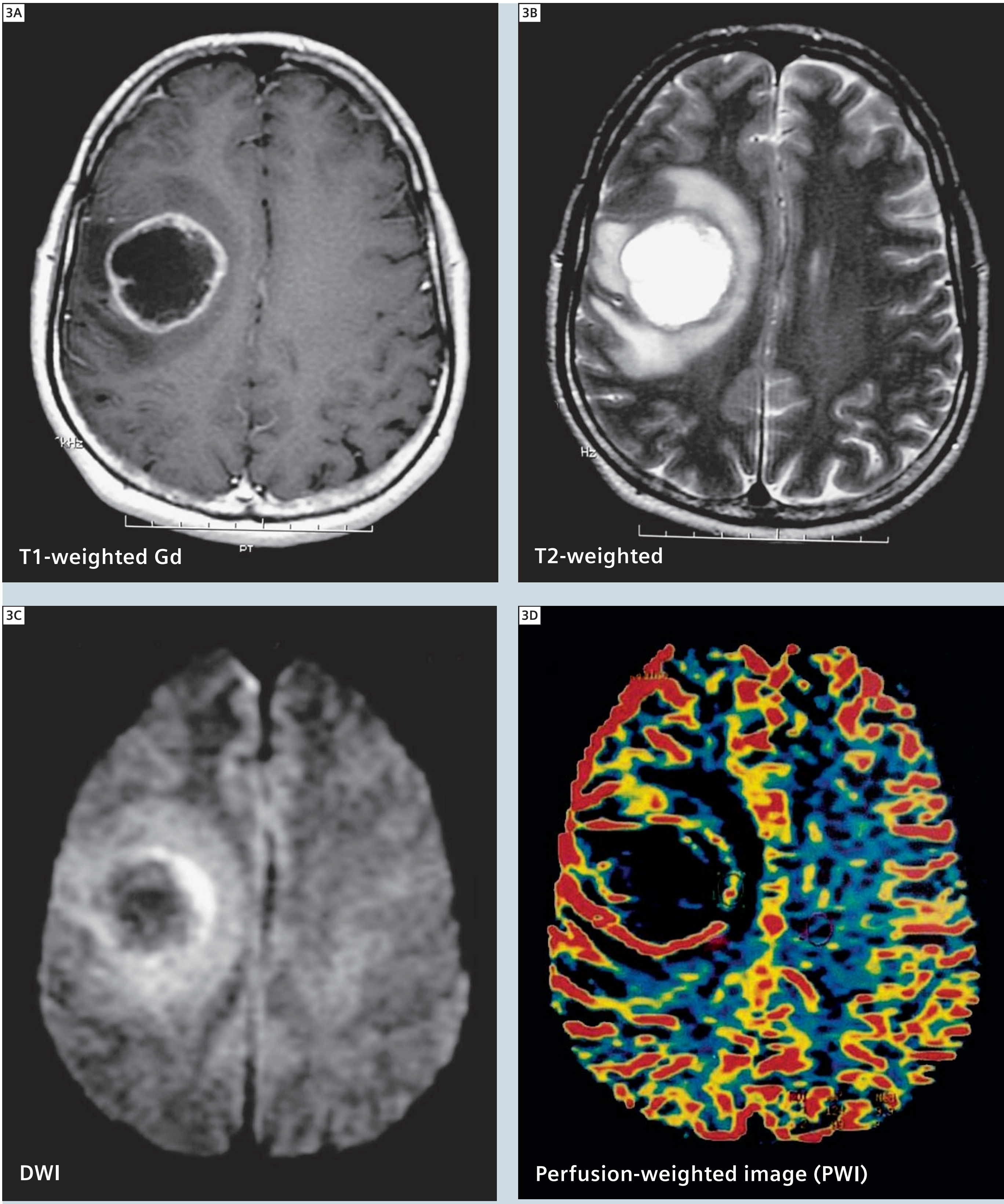
DWI is also an effective way of differentiating an arachnoid cyst from epidermoid tumors. Both lesions present similar signal intensity characteristic of cerebrospinal fluid (CSF) on T1 and T2 sequences. On DWI, epidermoid tumors are hyperintense – for they are solidly composed – whereas arachnoid cysts are hypointense, demonstrating high diffusivity. The ADC values of epidermoid tumors are similar to those of the brain parenchyma, whilst ADC values of arachnoid cysts are similar to those of CSF.

In certain settings diffusion-weighted imaging can increase both the sensitivity and specificity of MR imaging in the evaluation of brain tumors by providing information about tumor cellularity, which may in turn improve prediction of tumor grade. The mechanism in which DWI may help in the tumor grading is based on the fact that free water molecule diffusivity is restricted by cellularity increase in high-grade lesions. The reduction in extracellular space caused by tumor cellularity causes a relative reduction in the apparent diffusion coefficient (ADC) values. Perhaps most helpfully, high grade tumors have in some studies been found to have low ADC values, suggesting a correlation between ADC values and tumor cellularity. In some studies, however, ADC values found in high- and low-grade gliomas have overlapped somewhat. It is well known that the brain tumors, specially the gliomas, are heterogeneous. Usually within a same neoplasm grade, mostly high-grade, different histologic features of grades II–IV are presented. This limitation may also be explained by the fact that it is not only the tumor cellularity that is responsible for reducing the diffusibility.

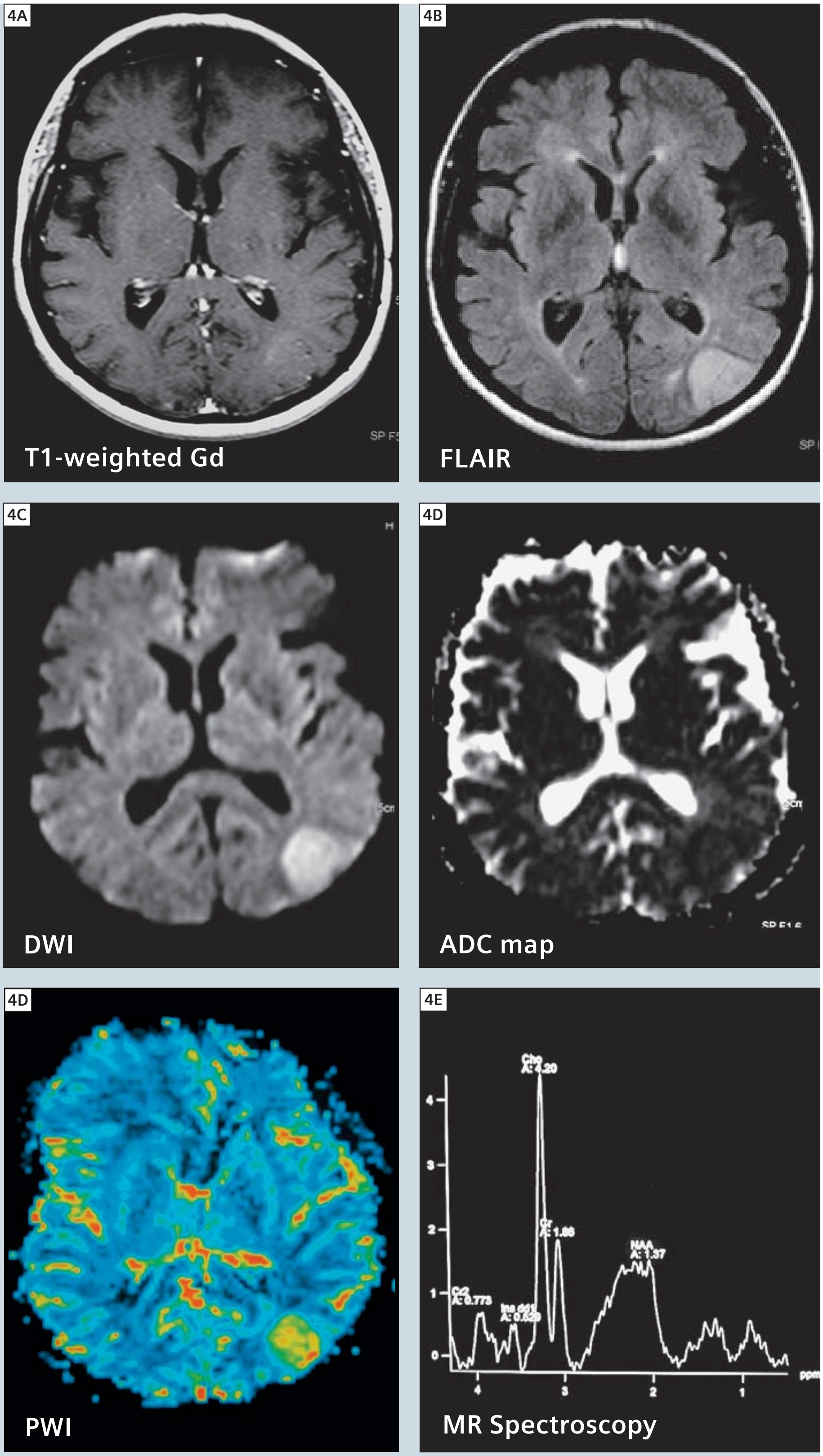
Lymphoma, a highly cellular tumor, has hyperintensity on DWI and reduced ADC values. While meningiomas also have a restricted diffusion, displaying low ADC values, they rarely present difficulty in diagnosis. DWI can be somewhat helpful in distinguishing medulloblastoma from other pediatric brain tumors, as it seems to display restricted diffusion presumably because of the densely packed tumor cells and high nuclear-to-cytoplasm ratio. The solid enhancing portion of cerebellar haemangioblastomas demon-



2 A bilobulated ring enhancing necrotic lesion, surrounded by vasogenic edema, demonstrating restricted diffusion within the lesion.
Diagnosis: Abscess



3 An expansive ring enhancing cystic/necrotic lesion, surrounded by vasogenic edema/infiltrative lesion, demonstrating restricted diffusion and high perfusion in its borders and unrestricted diffusion within the lesion.
Diagnosis: Glioblastoma Multiforme (GBM)



4 A non-enhancing cortical lesion, with high perfusion and restricted diffusion. MR-spectroscopy demonstrates a very high choline peak and low NAA.
Diagnosis: Anaplastic astrocytoma

strates high diffusibility, due to its rich vascular spaces.

Diffusion-Tensor MR image

The movement of water occurs in all three directions, and is assumed to behave in a manner physicists can describe using a Gaussian approximation. When water molecules diffuse equally in all directions, this is termed isotropic diffusion. In the white matter, however, free water molecules diffuse anisotropically, that is to say the water diffusion is not equal in all three orthogonal directions. The fractional anisotropy (FA) measures the fraction of the total magnitude of diffusion anisotropy. In addition to assessment of the diffusion in a single voxel, DTI has been used to attempt to map the white matter fiber tracts. A color-coded map of fiber orientation can also be determined by DTI. A different color has been attributed to represent a different fiber orientation along the three orthogonal spatial axes.

The precise determination of the margins of the tumor is of the utmost importance to the management of brain tumors. The goal of a surgical approach to the brain neoplasm is the complete resection of the tumor, coupled with minimum neurological deficit.

Since it is generally accepted that conventional MR imaging underestimates the real extent of the brain tumor, given its ability to verify neoplastic cells that infiltrate peritumoral areas of abnormal T2-weighted signal intensity, many practitioners are uncomfortable using only conventional MRI approaches. While this remains to be proven, it does appear from straightforward inspection that DTI is able to illustrate the relationship of a tumor with the nearby main fiber tracts. Because of this, many have begun to suggest that DTI might be used to aid in surgical planning and possibly aid radiotherapy planning, as well as to monitor the tumor recurrence and the response to the treatment.

Based on these findings, DTI seems to be of great value in the detection of FA values, variation in pure vasogenic edema and the combination of vasogenic edema

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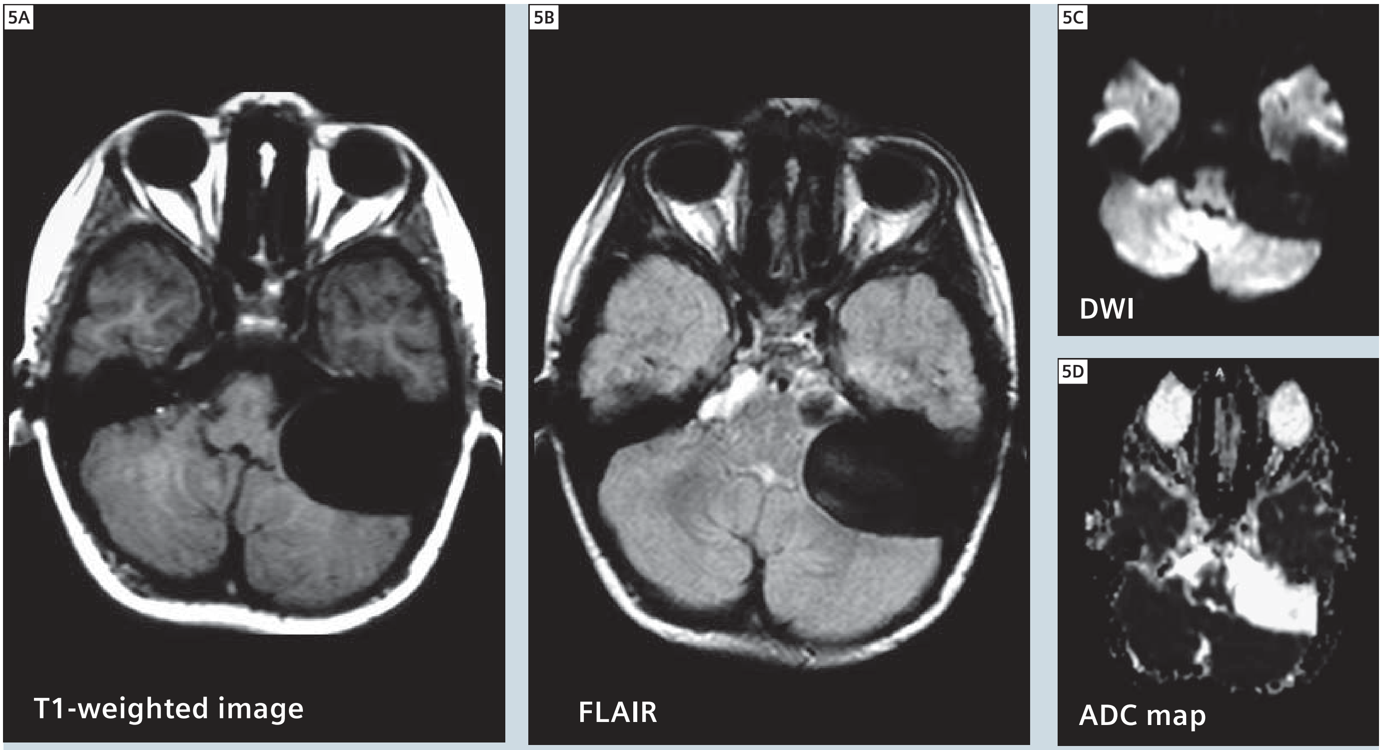
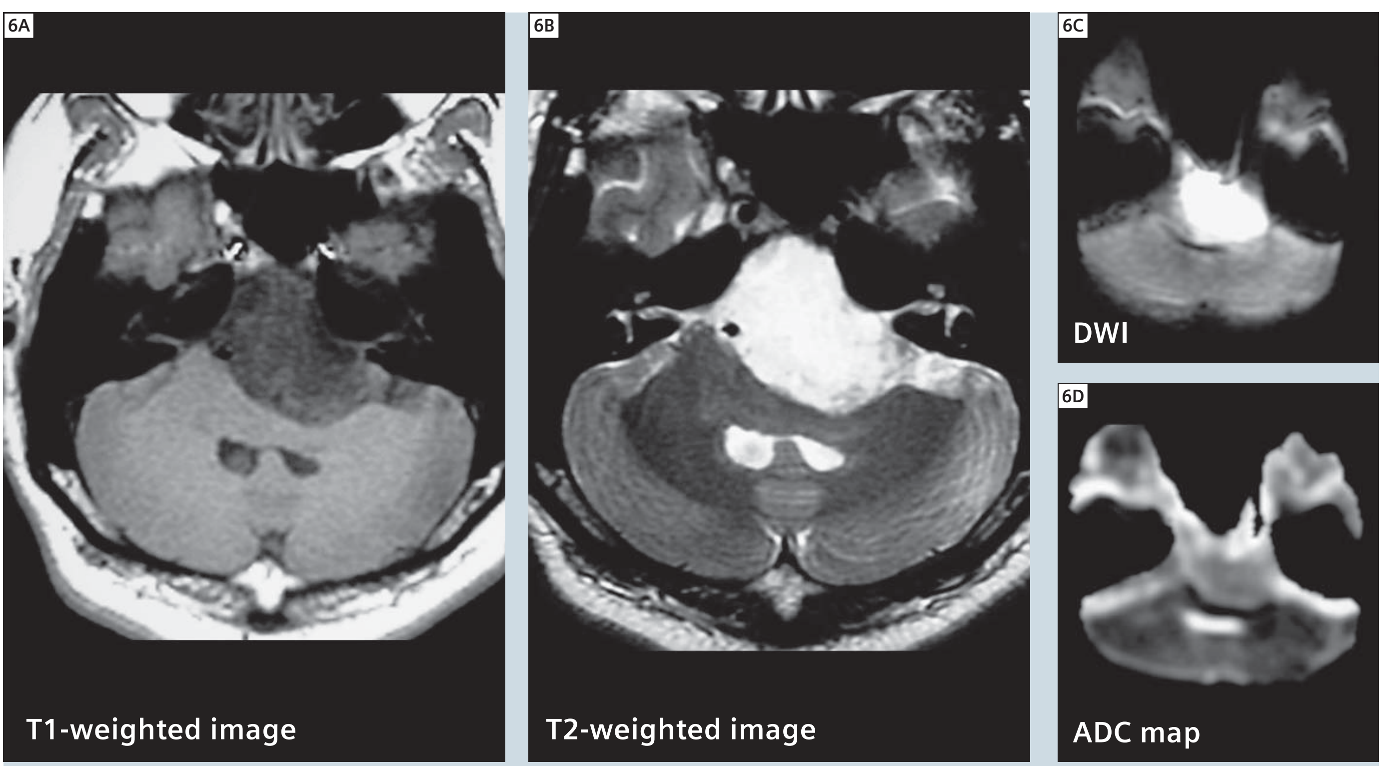
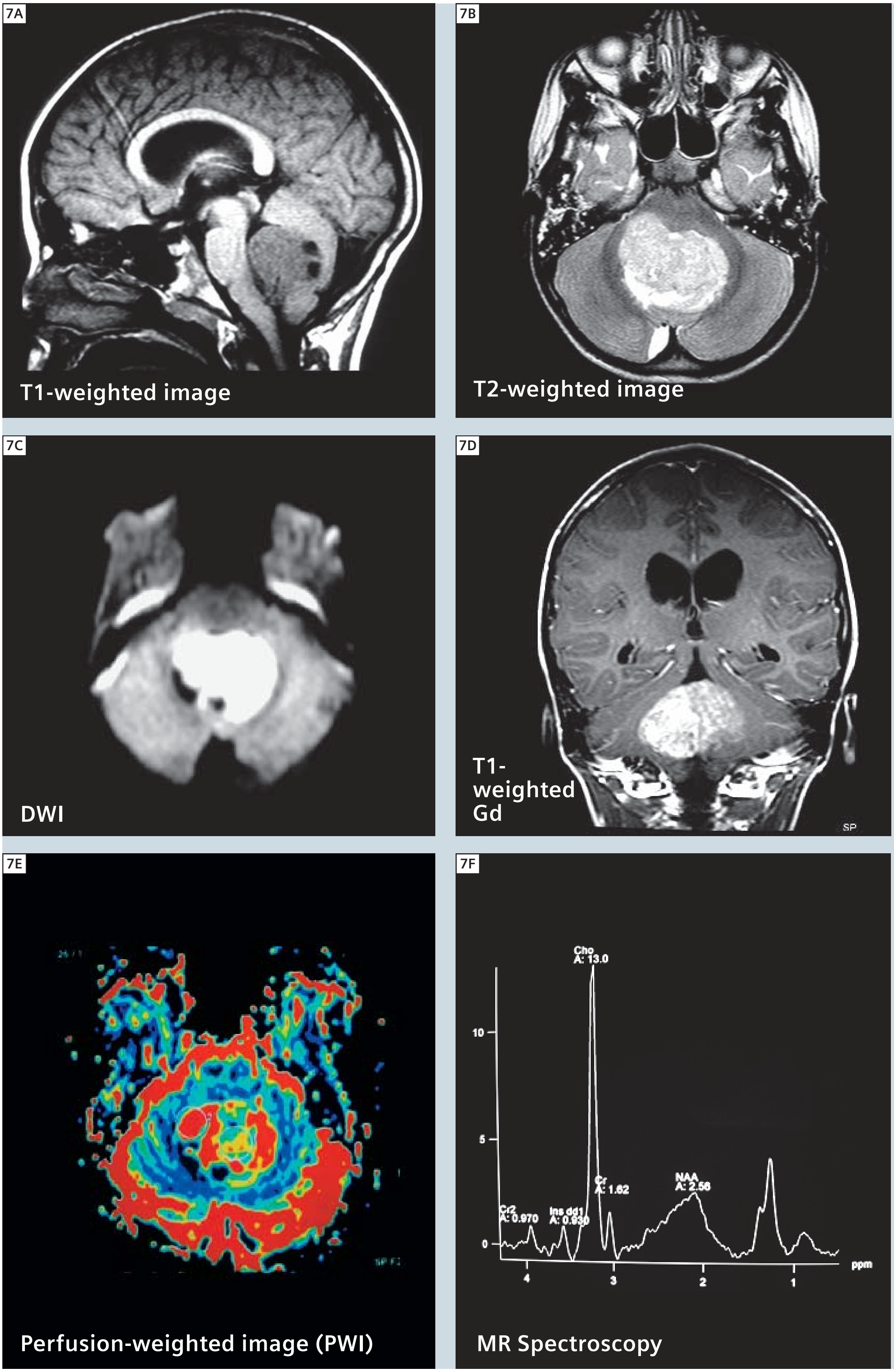


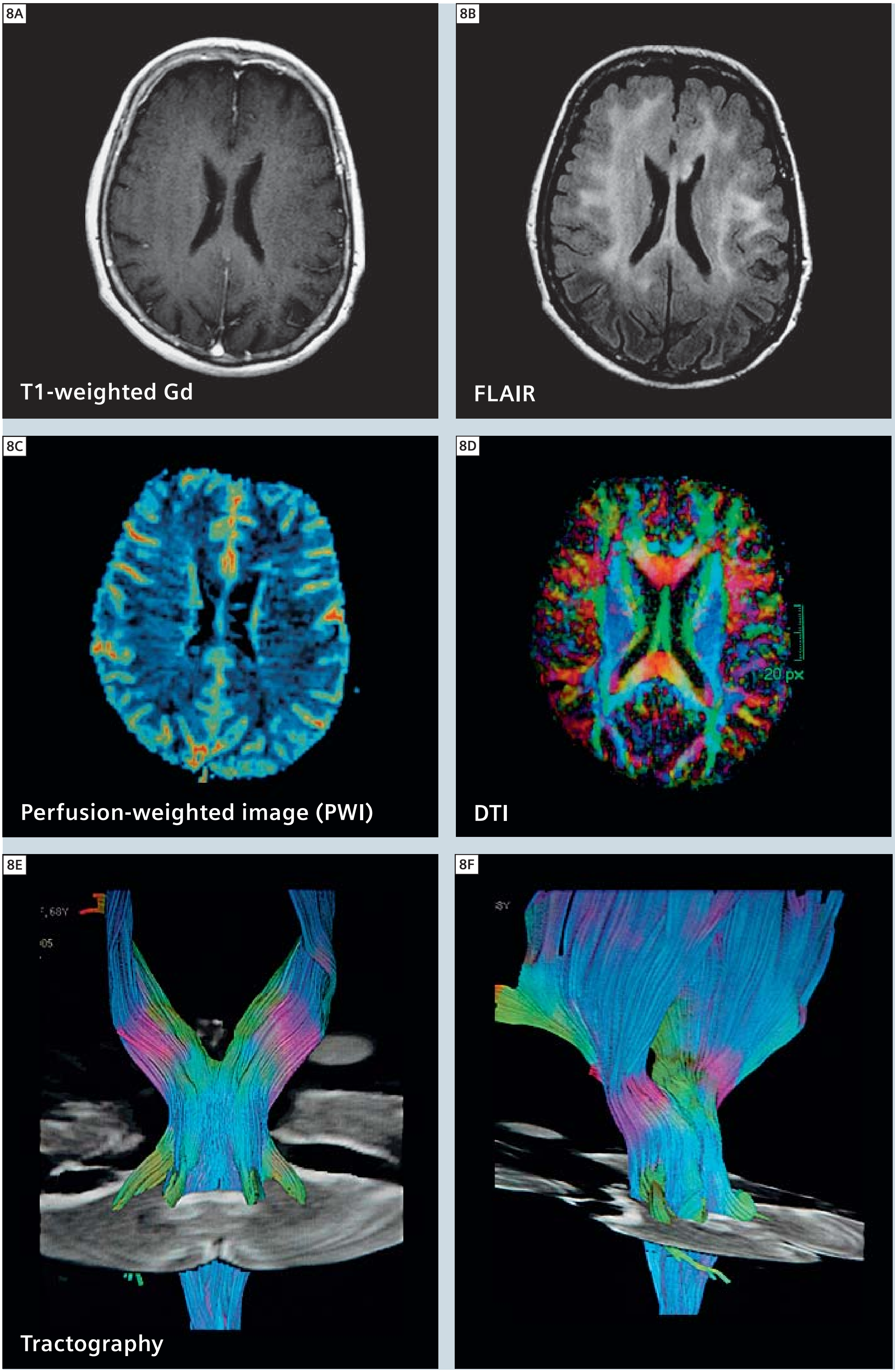
5 An expansive lesion in the left aspect of the posterior fossa, demonstrating similar signal intensity to CSF and high diffusibility.
Diagnosis: Arachnoid cyst



6 An expansive lesion in the left aspect of the posterior fossa, demonstrating similar signal intensity to CSF and high signal intensity on diffusion-weighted imaging (DWI). **Diagnosis:** Epidermoid



7 An expansive intraventricular enhancing lesion in the fourth ventricle, demonstrating restricted diffusion, hyperperfusion and a very high Choline peak, low NAA and lipids/lactate peak. **Diagnosis:** Medulloblastoma



8 An infiltrative, non-enhancing white matter lesion, without hyperperfusion. Diffusion Tensor Imaging (DTI) demonstrates a reduction in FA values, preserving the direction of the main fiber tracts. **Diagnosis:** Gliomatosis cerebri and extracellular matrix destruction. In conclusion, DTI may be able to distinguish high-grade gliomas from low-grade gliomas and metastatic lesions.

Pre-surgical planning

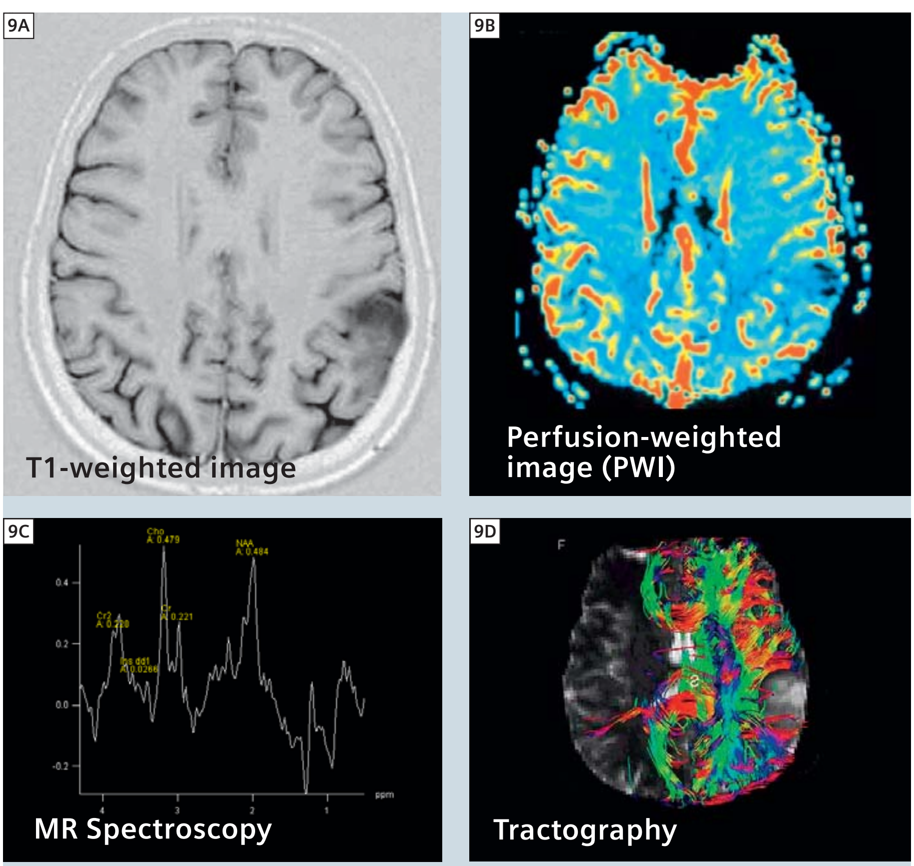
DTI appears to be the only non-invasive method of obtaining information about the fiber tracts and is able to suggest them three-dimensionally, though the validity of these suggestions remains to be carefully studied. Frequently, the involvement of the white matter tracts can be clearly identified in brain tumor patients by using both anisotropic maps (FA maps are the most widely used) and tractography. Based on DTI findings, resulting from studies of brain tumor patients, the white matter involvement by a tumor can be arranged into five different categories:

- Displaced: maintained normal anisotropy relative to the contralateral tract in the corresponding location, but situated in an abnormal T2-weighted signal intensity area or presented an abnormal orientation.
- Invaded: slightly reduced anisotropy without displacement of white matter architecture, remaining identifiable on orientation maps.
- Infiltrated: reduced anisotropy but remaining identifiable on orientation maps.
- Disrupted: marked reduced anisotropy and unidentifiable on oriented maps.
- Edematous: maintained normal anisotropy and normally oriented but located in an abnormal T2-weighted signal intensity area.

In short, DTI is gaining enthusiasm as a pre-operative MRI method of evaluating brain tumors closely related to eloquent regions. DTI appears to be particularly advantageous for certain types of surgical planning, optimizing the surgical evaluation of brain tumors near white matter tracts. Formal studies that demonstrate that DTI can successfully prevent post-operative complications have yet to be carried out but preliminary data appear promising.

Intracranial neoplasms may involve both the functional cortex and the corresponding white matter tracts. The preoperative identification of eloquent areas through noninvasive methods, such as blood-oxygen-level-dependent (BOLD) functional MR imaging (fMRI) and DTI tractography, offers some advantages.

Increasingly, investigators are beginning to combine fMRI with DTI: this might allow us to precisely map an entire functional circuit. Even though fMRI locates eloquent cortical areas, the determination of the course and integrity of the fiber tracts remains essential to the surgical planning.



9 An expansive cortical lesion, with hypoperfusion. MR-spectroscopy demonstrates a high Choline peak and low NAA. The lesion seems to dislocate the main adjacent fiber tracts. **Diagnosis:** Low grade Glioma

Limitations

While initial reports suggest advantages of DWI and DTI in the evaluation of patients with brain tumors, these reports are largely single-center, uncontrolled, preliminary findings. Therefore these results must be cautiously interpreted. Furthermore, there remain substantial technical hurdles, even though the rapid evolution of MRI systems is making ever more powerful approaches possible. Such improvements are particularly welcome given the limited signal-to-noise ratio of diffusion overall. Nevertheless, these initial data are promising.

Summary

Diffusion imaging appears to have the potential to add important information to pre-surgical planning. While experience is limited, DTI appears to provide useful local information about the structures near the tumor, and this appears to be useful in planning. In the future, DTI may provide an improved way to monitor intraoperative surgical procedures as well as their complications. Furthermore, the evaluation of the response of treatment to chemotherapy and to radiation therapy might also be possible. While diffusion imaging has some limitations, its active investigation and further study are clearly warranted.

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