Advanced MR Imaging in Pediatric Brain Tumors, Clinical Applications

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KEYWORDS

• MR • Advanced imaging • Pediatric • Brain tumor

KEY POINTS

- A combination of conventional and advanced MR imaging sequences is recommended to make the correct diagnosis in pediatric patients suspected to have a brain tumor.
- In the work-up of brain tumors at least diffusion-weighted imaging/diffusion tensor imaging, MR spectroscopy (MRS), and a perfusion MR technique should be included in the imaging protocol.
- MRS data may play an important role in assessing therapeutic response and therefore should be interpreted by experienced neuroradiologists.
- Arterial spin labeling is a promising noninvasive perfusion sequence that may become an important biomarker for tumor diagnosis and tumor grading.
- Future advances in molecular biology will alter neuroradiologic concepts and thinking and add information to that obtained from conventional and advanced MR imaging techniques, which will benefit pediatric patients with brain tumors.

INTRODUCTION

Imaging of brain tumors has significantly improved with the use of advanced magnetic resonance (MR) techniques, such as MR spectroscopy (MRS), perfusion-weighted imaging, diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), susceptibility-weighted imaging (SWI), and functional MR (fMR) imaging.[1–10] Conventional MR imaging techniques provide anatomic/structural information about the brain. Unlike conventional imaging, advanced MR techniques also provide physiologic and functional information concerning metabolism; hemodynamics; and, with diffusion-weighted technique, information on brain tumor cellularity. Recently, the introduction of DNA methylation profiling for molecular classification has been proposed, which outperforms the current histopathologic classification and thus might serve as a basis for the next World Health Organization classification scheme for central nervous system (CNS) tumors. In the future, this may have a great impact on the correlation between advanced imaging assessment and the newly proposed molecular classification. This overview is based on the literature between the currently used histopathologic classifications of pediatric brain tumors and their characteristics on advanced MR imaging techniques. In the near future it will be mandatory to scan with advanced imaging protocols in all pediatric brain tumors, classified by their molecular phenotype to reevaluate their diagnostic value.

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The most useful clinical applications of these advanced MR techniques in pediatric brain tumors, stratified by the current classification, are discussed here.

1. DWI approaches (DWI, DTI, diffusion kurtosis imaging [DKI])
2. MRS (single-voxel [SV] imaging, and chemical shift imaging [CSI])
3. Perfusion-weighted techniques (dynamic susceptibility contrast [DSC] technique; dynamic contrast-enhanced [DCE]; and arterial spin labeling [ASL], a noncontrast technique)
4. Other advanced MR imaging sequences, useful for diagnosis and presurgical planning in children suspected to have a brain tumor (SWI and fMR imaging)

Diffusion-Weighted Imaging Technique (Diffusion-Weighted Imaging, Diffusion Tensor Imaging, Diffusion Kurtosis Imaging)

DWI is commonly used by (pediatric) neuroradiologists in everyday clinical practice. Although it is no longer a novel imaging technique, it provides information that is not obtainable using conventional MR sequences and is therefore discussed in this article.

The additional information is obtained by measuring the mobility of water molecules, assuming a process of random, unrestricted, but potentially hindered diffusion. The diffusion probability distribution function, the chance of a particular proton diffusing from one location to another in a given time, is thus considered a gaussian distribution, with the standard deviation relating to the apparent diffusion coefficient (ADC). The ADC value depends on the complexity of the cytoarchitecture, determined by, for example, cell membranes, intracellular organelles, and the rapid exchange of protons between different compartments (**Fig. 1**). The cytoarchitecture of the tumor can inhibit random brownian motion and thus causes water diffusion to deviate from strict gaussian behavior. This restricted diffusion appears hyperintense on the diffusion trace map and dark on the ADC map (**Fig. 2**). In clinical practice and research, ADC maps and ADC values have been used to assess tumor cellularity and tumor grade (**Fig. 3**). Recently, Poretti and colleagues[4] showed that tumor grade as estimated by ADC values could be better assessed only from the solid, contrast-enhancing part of the tumor rather than the entire tumor. Further, ADC values can also be used to assay treatment response and detect tumor recurrence and even to differentiate tumor recurrence from pseudoprogression.[5]

Although mainly used in the treatment scheme of high-grade gliomas in adults, antiangiogenic drugs may also be a treatment option in pediatric patients with brain tumors. DWI based on ADC analyses is less affected by vascular permeability changes caused by antiangiogenic treatment than contrast-enhanced T1-weighted imaging and is therefore a good imaging marker of treatment outcomes. However, clinicians should beware of areas of restricted diffusion that may appear after antiangiogenic treatment, which were stable on follow-up MR imaging studies, and therefore are more consistent with necrosis than tumor recurrence/progression.[6]

There are studies focusing on treatment-induced changes in ADC values by comparing pretreatment and early posttreatment measures.[7] Some reports even advocate the use of functional diffusion map methods by voxel-wise subtraction of the pretreatment and posttreatment ADC maps for accurate assessment of changes in ADC values at all tumor locations.[8] Also ADC value changes over time, suggesting that serial MR (DWI) imaging may be useful to investigate possible changes in volume of low-ADC regions within the tumor.

Although the results from DWI and quantitative ADC look promising and DWI imaging is easy and quick to perform, clinicians should keep in mind that variations in equipment (even from the same brand) and acquisition parameters can result in significant differences in calculated ADC values. Even using ratios by comparing with normal-appearing brain tissue as a reference may produce inconsistent results. This possibility is especially important in follow-up scanning, making it sometimes more difficult to differentiate between tumor growth and necrosis. Second, brain tumors may become more heterogeneous after treatment, which may influence ADC values and result in inaccurate diagnosis of tumor progression. Some investigators suggest histogram-based methods but this is a time-consuming approach.[9]

Diffusion tensor imaging

The diffusion-weighted technique not only uses the magnitude of the diffusion but can also provide the direction of diffusion and is therefore sensitive to directional movements of water molecules using DTI. DTI has been used extensively for the identification of functional white matter tracts in vivo. In neuro-oncology, DTI has the potential to establish spatial relationships between normal-appearing white matter and tumor borders and provide clinically valuable information on