Clinical Application of MR Spectroscopy and Imaging of Brain Tumor

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Advanced imaging techniques, including diffusion tensor imaging (DTI), perfusion-weighted imaging (PWI), and magnetic resonance spectroscopy (MRS) can provide more information than that regarding anatomy. These techniques have been commonly used in the clinical field and recently been shown useful in diagnosing brain tumors, especially in cases difficult to specify using conventional imaging. Differentiation requires more than attention to each advanced image. Diagnostic accuracy improves by combining information from MRS with that from other sequences, such as maps of apparent diffusion coefficient (ADC) and fractional anisotropy (FA) generated from DTI and of cerebral blood volume (CBV) generated from PWI.

We show clinical applications of advanced imaging techniques, combined MRS, for brain tumor.

Keywords: brain tumor, magnetic resonance spectroscopy, perfusion-weighted image, advanced imaging

Introduction

In addition to conventional magnetic resonance (MR) imaging techniques, advanced techniques including diffusion tensor imaging (DTI), perfusion-weighted imaging (PWI) and magnetic resonance spectroscopy (MRS) can provide information regarding more than anatomy and have been commonly used in the clinical field. Maps of apparent diffusion coefficient (ADC), fractional anisotropy (FA), and regional cerebral blood volume (rCBV) as well as 1H-MRS generated by advanced techniques aid specification of brain tumors.1,2

Use of scanners with high magnetic field has improved image quality of MRS and increased its role in the diagnosis and management of intracranial tumors. 1H-MRS can provide metabolic information, including that regarding tissue activity or brain damage correlating with pathological changes. High choline (Cho) and low N-acetyl-aspartate (NAA) peaks show tumor aggressiveness, and other metabolic peaks such as lipid (Lip) or lactate (Lac) can also show necrosis in tumor. Though MRS has been popular, acquisition of good metabolic peak is negatively affected by such problems as chemical shift effects, influence from lipids, insufficient water suppression, or inadequate shimming.

Combining images from MRS with those from other advanced techniques, including CBV maps generated from PWI, is reported to improve diagnostic accuracy for intraaxial brain tumors.3,4 CBV map can be generated from dynamic susceptibility contrast T2*-weighted gradient-echo planar PWI (DSC-PWI) acquired during the first pass of the standard dose of gadopentetate dimeglumine contrast agent. Tumor blood volume (TBV) value can be measured from the CBV map, and TBV values have been correlated to tumor grade and vascularity, with higher TBV values associated with gliomas of higher grade.5–7

Al-Okaili and colleagues suggested using advanced MR imaging for diagnosis.1,2 They first classified contrast enhancement into 2 groups and specified diagnosis by referring to other advanced imaging results (Fig. 1).

We also show clinical applications of advanced
MR imaging combined MRS for common brain tumors, which we have classified by presence or absence of enhancement.

**Advanced Imaging Features in Enhancing Tumor**

On contrast-enhanced T₁-weighted images (ce-T₁WI), high grade glioma (HGG), lymphoma and metastasis show enhancement, and it is sometimes difficult to specify using conventional MR images. Among these tumors, HGG has shown the highest TBV value because of its strong neoangio genesis.⁸,⁹ The maximum TBV value is usually applied and normalized to a region of interest in normal white matter. A relative TBV (rTBV) value of 1.75 has been suggested as a cutoff threshold for distinguishing high from low grade neoplasm,¹⁰ with a lower rTBV value serving as a good predictor for outcome.¹¹ On MRS, HGG is characterized by elevated both Cho and Lip/Lac peaks and reduced NAA peak that represent tumor aggressiveness (Fig. 2). Interestingly, demonstration of this abnormal metabolic peak also showed in normal-appearing surrounding tissue, represents tumor infiltration (Fig. 3).

In immunocompetent patients, lymphoma usually shows homogeneous hyperintensity on T₂-weighted (T₂WI) and fluid-attenuated inversion-recovery (FLAIR) images and is homogeneously enhancing on ce-T₁WI (Fig. 4a–c). On diffusion-weighted images (DWI), lymphoma is known to show hyperintensity with decreased apparent diffusion coefficient (ADC) that reflects a higher nuclear/cytoplasm ratio (Fig. 4d, e).¹² TBV of lymphoma was normal to slightly increased compared to the TBV of HGG (Fig. 4f).⁸,⁹ On MRS, the peak pattern was similar with other malignant glioma (Fig. 4g, h).

On conventional MR imaging, the signal pattern
Fig. 2. A 78-year-old man with glioblastoma multiforme
The tumor, located in the left temporal lobe, showed heterogeneous hyperintensity on fluid-attenuated inversion-recovery (FLAIR) (a), hypointensity on T1-weighted imaging (T1WI) (b) and ring enhancement on contrast-enhanced T1-weighted imaging (ce-T1WI) (c). Diffusion-weighted imaging (DWI) showed an area of restricted diffusion in the tumor (d). The hypervascular lesion on the cerebral blood volume (CBV) map appeared as an area of hyperintensity that corresponded to the lesion with contrast enhancement (e). On magnetic resonance spectroscopy (MRS) with intermediate echo time (TE, 144 ms), increased choline (Cho) and decreased N-acetylaspartate (NAA) appeared in the peripheral enhancing lesion of the tumor (f) (g; contralateral normal white matter).

of metastatic brain tumor varies depending on the character of the primary tumor but generally demonstrates ring enhancement. Compared to the TBV of HGG, the degree of increased TBV value of metastatic brain tumor was reported to be smaller. On MRS, the presence and absence of NAA and Lip/Lac peaks were useful for specification. In patients with metastasis, a Lip/Lac peak was observed in the entire lesion, with no NAA peak in the inner region, whereas the same pattern was observed in only 10% of glioblastoma cases (Fig. 5). A Cho/NAA ratio of 1.0 has also been
reported to demonstrate 100% accuracy for differentiating primary and secondary neoplasms.\textsuperscript{14}

**Advanced Imaging Features in Non-enhancing Tumor**

Low grade gliomas (LGG), such as astrocytoma and oligodendroglioma, commonly show faint hyperintensity on T\textsubscript{2}WI and FLAIR, are nonenhancing on ce-T\textsubscript{1}WI, have a decreased rTBV value, and demonstrate a normal MRS peak pattern in tumor (Fig. 6).

An important exception among LGGs is tumors with oligodendrogial features that may have elevated TBV values, which has been observed in particular in low-grade oligodendroglial and oligoastrocytomas with 1p 19q deletion.\textsuperscript{15} Cases with suspected oligodendroglial features require special attention to this characteristic tumor behavior.

In occasional cases of nonenhancing high grade gliomas, advanced age along with imaging findings of heterogeneity, edema, mass effect, necrosis, and cystic formation, generally favor high grade histology.\textsuperscript{16,17} In addition, contrast enhancement on T\textsubscript{1}WI is considered a strong predictor of malignancy,\textsuperscript{18} whereas homogeneous nonenhancing masses are typically low grade. However, about nine to 45% of homogeneous nonenhancing supratentorial gliomas are malignant,\textsuperscript{19–25} suggesting that diagnostic MR imaging features alone are unreliable for predicting the grade of nonenhancing brain neoplasms because the features provide no information on tumor microvascularity, angiogenesis, metabolism, or micronecrosis.\textsuperscript{26–28}

Increased TBV values have been reported prior to appearance of contrast enhancement on T\textsubscript{1}-weighted MR images. At some stage in the malignant transformation of astrocytomas, increased vascularity within the neoplasm may precede disruption of the blood-brain barrier, possibly rendering TBV measurements an early predictor of malignant transformation. The rate of change in TBV values was significantly higher in malignant transformers than nontransformers, in which the rate of change remained relatively stable and increased only slightly.\textsuperscript{29} MRS can also show possible malignancy, which is represented by higher levels of Cho/NAA and Lip/Lac within the tumor (Fig. 7). Both findings strongly suggest malignant potential.

**Conclusions**

Though some problems remain in using recent advanced imaging techniques for diagnosing brain neoplasms, their images can provide more information than those from conventional imaging. Therefore, we should apply the advanced techniques as much as possible, especially in cases difficult to specify by conventional images.

**References**

Fig. 4. An 82-year-old man with lymphoma of the central nervous system (CNS)
The tumor showed homogeneous hyperintensity on fluid-attenuated inversion-recovery (FLAIR) (a) and hypointensity on T₁-weighted imaging (T₁WI) (b), and as an area of partial enhancement in the tumor (e). Diffusion-weighted imaging (DWI) showed hyperintensity with decreased apparent diffusion coefficient (ADC), which represented restricted diffusion (d, e). The tumor showed iso- to slightly hyperintensity on the cerebral blood volume (CBV) map (f). Magnetic resonance spectroscopy (MRS) with short echo time (TE, 30 ms) demonstrated increased choline (Cho) and decreased N-acetylaspartate (NAA) in the tumor and lipid/lactate (Lip/Lac) peak (g), similar to findings of high grade glioma. Tissue surrounding the tumor lesion appeared normal (h).
Fig. 5. A 55-year-old man with brain metastasis from lung cancer (adenocarcinoma)
In preoperative images, the tumor showed hyperintensity on fluid-attenuated inversion-recovery (FLAIR) (a-1) and ring enhancement with cystic component on contrast-enhanced T1-weighted imaging (ce-T1WI) (a-2). After surgery, the tumor was resected completely (b-1, 2). At one-year follow-up, ring enhancement with an irregular rim appeared adjacent to the postoperative lesion, and there was surrounding edema in the left parietoanterior lobe (c-1, 2). Increased tumor blood volume (TBV) and markedly increased lipid/lactate (Lip/Lac) peak on magnetic resonance spectroscopy (MRS) with short echo time (TE, 30 ms) could be seen in correspondence with the peripheral enhancing rim (d, e).

8. Hakyemez B, Erdogan C, Bolca N, Yildirim N,
A 39-year-old woman with oligodendrogliaoma

The tumor, located in the right frontal lobe, showed heterogeneous hyperintensity on fluid-attenuated inversion-recovery (FLAIR) (a) and was non-enhancing (b, c). Diffusion-weighted imaging (DWI) showed mild hyperintensity (d) and no hyperintensity on the cerebral blood volume (CBV) map in the tumor (e). On magnetic resonance spectroscopy (MRS) with short echo time (TE, 30 ms), the peak pattern in the tumor (f) resembled that in the contralateral normal white matter (g).


Fig. 7. A 64-year-old man with anaplastic astrocytoma
On fluid-attenuated inversion-recovery (FLAIR) (a), an area of homogeneous hyperintensity with slight enhancement (b, c) was seen in the left temporal lobe. Though the degree of enhancement in the tumor was weak, the tumor blood volume (TBV) was obviously increased, which means it contained malignant potential (d). Magnetic resonance (MR) spectroscopy with short echo time (TE, 30 ms) also showed the possibility of malignancy, with increased choline (Cho), decreased N-acetylaspartate (NAA), and highly increased lipid/lactate (Lip/Lac) peak in the tumor (f). (e: surrounding white matter)


