Amide Proton Transfer (APT) Imaging for Grading of Glioma

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TARGET AUDIENCE

Scientists and physicians who are interested in molecular imaging of brain tumors using a novel MRI method.

Introduction

Astrocytomas are the most common primary tumor in brain. It account for 30-40% among the intracranial tumors. Although contrast-enhanced T1-weighted MR imaging may grade the degree of tumor malignancy, studies have demonstrated that the degree of contrast enhancement is not a reliable biomarker of the tumor maligancy[1]. Amide proton transfer (APT) MR imaging can detect the molecular signals which are based on endogenous mobile proteins and peptides[2]. The previous studies have shown that APT can define the different components of the tumor and may differentiate between recurrence of tumor and radiation necrosis[3,4]. The purpose of this study is to investigate the role of the APT MR imaging for grading of glioma.

Methods

33 patients (18 male，15 female，age from 18 to 71 years with mean age of 40 years) were investigated and confirmed to have a glioma by postoperative pathology, in whom 3T MRI with T2-weighted, FLAIR, pre- and post-contrast T1-weighted and APT sequences were performed. For each patient, APT values of each regions of interest (ROI) were calculated and used for grading. Comparisons between APT values of high-grade (HGG) and low-grade gliomas (LGG) were performed. APT signals were calculated using a magnetization transfer ratio (MTR)-asymmetry analysis at ±3.5ppm. MRI results were validated with pathology.

Results

33 patients included 10 grade II, 11 grade III, and 12 grade IV tumors. Fig. 1 shows the typical characteristics of these gliomas of different grades. APT hyperintensity (compared to the contralateral white matter, cnawm) is a typical feature of high-grade (grade III and IV) brain tumors, independent of Gd enhancement. However, in patients with low-grade gliomas, the APT signal was consistently low. The average APT signal intensities were significantly higher in the tumor cores both in grade-III and grade-IV gliomas than in the low-grade glioma and the cnawm ($P < 0.01$; Fig. 2). However, there was no significant difference between grade III and IV ($P = 0.1$).

Discussion

APT imaging is recently emerged as a new contrast mechanism for MRI, which can detect endogenous cytosolic proteins and peptides through saturation of the amide protons in the peptide bonds. Our preliminary results in this study have shown that APT imaging may help identify the different grade of the tumor. In high-grade gliomas, the viable, actively growing tumor cores demonstrated high signal intensities on the APT images, in line with expectations based on increased content of cellular proteins in the lesion. Although some tumors do not enhance on the gadolinium-enhanced T1-weighted images, the high signal intensities still exist in the tumors on the APT images.

Conclusion

These data indicate the great potential of the APT signal as a valuable surrogate biomarker for identifying the pathological grade of brain tumors for tumor detection, diagnosis, and local therapy.

References

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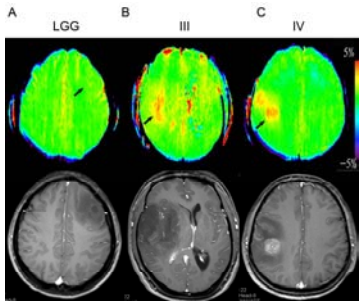

Fig 1. (A) Oligodendrocytoma (WHO grade II) of the left frontal lobe in a 27-year-old women was not enhanced with post-contrast T1WI. The APT signal intensity was low (arrow). (B) Anaplastic astrocytoma in a 39-year-old man (grade III). There was a minor enhancement in tumor core in post-contrast T1-weighted image, but a obviously high signal intensity on the APT image (arrow). (C) Glioblastoma multiforme in a 37-year-old man (grade IV). There were two enhancing tumor cores in the post-contrast T1WI image, which were hyperintense in the APT image (arrow).

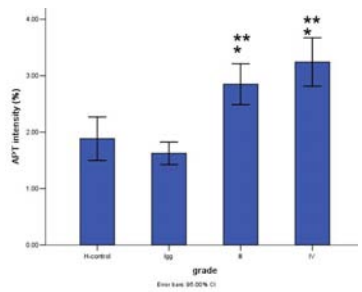

Fig. 2 Mean APT intensities of tumor cores in different grades of glioma and cnawm of high-grade glioma. APT signal was significantly higher in HGG than in LGG and cnawm. *, compared with cnawm; **, compared with LGG; $p<0.01$ in both. No difference was observed between grade III and IV.