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Assesment of perfusion in glial tumors with arterial spin labeling; comparison with dynamic susceptibility contrast method

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ABSTRACT

Purpose: Arterial spin labeling perfusion imaging (ASL-PI) is a non-invasive perfusion imaging method that can be used for evaluation and quantification of cerebral blood flow (CBF). Aim of our study was to evaluating the efficiency of ASL in histopathological grade estimation of glial tumors and comparing findings with dynamic susceptibility contrast perfusion imaging (DSC-PI) method.
Methods: This study involved 33 patients (20 high-grade and 13 low-grade gliomas). Multiphase multislice pulsed ASL MRI sequence and a first-passage gadopentetate dimeglumine T2*-weighted gradient-echo single-shot echo-planar sequence were acquired for all the patients. For each patient, perfusion relative signal intensity (rSI), CBF and relative CBF (rCBF) on ASL-PI and relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) values on DSC-PI were determined. The relative signal intensity of each tumor was determined as the maximal SI within the tumor divided by SI within symetric region in the contralateral hemisphere on ASL-PI. rCBV and rCBF were calculated by deconvolution of an arterial input function. Relative values of the lesions were obtained by dividing the values to the normal appearing symmetric region on the contralateral hemisphere. For statistical analysis, Mann–Whitney ranksum test was carried out. Receiver operating characteristic curve (ROC) analysis was performed to assess the relationship between the rCBF-ASL, rSI-ASL, rCBV and rCBF ratios and grade of gliomas. Their cut-off values permitting best discrimination was calculated. The correlation between rCBV, rCBF, rSI-ASL and rCBF-ASL and glioma grade was assessed using Spearman correlation analysis.
Results: There was a statistically significant difference between low and high-grade tumors for all parameters. Correlation analyses revealed significant positive correlations between rCBV and rCBF-ASL ($r = 0.81$, $p < 0.001$). However correlation between rCBF and rCBF-ASL was weaker ($r = 0.64$, $p < 0.001$).
Conclusion: Arterial spin labeling is an employable imaging technique for evaluating tumor perfusion non-invasively and may be useful in differentiating high and low grade gliomas.

1. Introduction

Brain tumors constitute one of the important disease group and frequently difficulties are encountered in imaging [1]. Glial tumors are the most common primary neoplasms of the brain in adults, and histopathological distribution of gliomas were complex between low grade and high grade [2]. Histopathological grading of brain tumors which is achieved by surgical excision or stereotactic biopsy is crucial for optimal treatment planning [3].

Magnetic resonance (MR) imaging in particular is the most frequently used imaging modality to evaluate brain tumors. In addition to conventional MR sequences, advanced MR techniques found their place in clinical practice. Perfusion imaging, diffusion-weighted imaging, and MR spectroscopic imaging are the commonly used advanced MR imaging methods for brain tumor evaluation. These advanced techniques generate physiological data and information on chemical composition [1].

In general, contrast-enhanced conventional cranial MR imaging is mostly sufficient for intracranial tumor diagnosis. But there are some limitations, like nonspecificity of contrast enhancement. Enhancement after contrast agent reflects blood brain barrier disruption rather than a true assessment of tumor vascularity.

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Especially, differential diagnosis between high and low-grade tumors and between radiation necrosis and recurrent tumors are challenges by using only conventional contrast-enhanced cranial MRI [4,5].

Recent advances in dynamic MR imaging have enabled the assessment of tumor vascularity quantitatively. Among various functional imaging techniques, perfusion MR imaging is particularly sensitive in demonstrating microvasculature and tumor neovascularization. Clinical applications of perfusion MR imaging in brain tumor evaluation include assessment of tumoral grade, achieving guidance for stereotactic biopsy, differentiation between recurrent glioma and radiation necrosis, and determination of prognosis and response to treatment [4,5].

Perfusion MR imaging methods exploit signal changes that accompany the passage of tracer through the cerebrovascular system. The tracer can be endogenous (arterial water) or exogenous (deuterium oxide, gadopentetate dimeglumine). Arterial spin labeling (ASL) MRI is a perfusion imaging method, which uses arterial blood water as a freely diffusible endogenous tracer [6]. One of the exogenous tracer methods of perfusion imaging is dynamic susceptibility contrast perfusion imaging (DSC-PI). In DSC-PI, rapid loss of MR signal on T2* weighted images is measured and then used to calculate the change in concentration of contrast material for each individual voxel [7].

The goal of our study was to determine the usefulness of ASL in evaluating the histopathological grade of cerebral gliomas and to compare findings with DSC-PI method.

2. Materials and methods

2.1. Patient population

This retrospective study included thirty-three patients with histopathologically proven gliomas (18 male, 15 female; age range = 17 to 74 years, mean age = 46.9 years) who had undergone perfusion MRI examination in our institute with both ASL and DSC perfusion imaging methods between January 2010 and May 2013. In total, we investigated twenty high-grade and thirteen low-grade gliomas. Histopathological diagnosis was obtained with surgical excision for all tumors. The grading of gliomas was based on 2007 World Health Organization brain tumor classification [8]. The study was approved by institutional ethical committee. The lesions were eighteen glioblastome multiforme, one grade 3 astrocytoma, one gliosarcoma, eleven grade 2 oligodendroglioma, one disembryoblastic neuroepithelial tumor (DNET), and one pilocytic astrocytoma.

2.2. Imaging protocol

All MR imaging examinations were performed on a clinical 3 Tesla MR imaging system (Philips Achieva 3T, Best, Netherlands) by using a 32 channel head coil. For conventional MR study, axial 3D turbo field echo (TFE) (TR/TE = 8.1/3.7 ms), axial T2-weighted turbo spin-echo (TSE) (TR/TE = 3000/80 ms), and axial post-contrast 3D-TFE images were acquired.

Multiphase ASL method was used in all patients. ASL-PI studies were performed after conventional MR sequences. ASL was capable of multisection image acquisition at multiple inversion time points (multiple TI) and was based on the EPISTAR pulsed ASL technique. On the basis of conventional MR imaging results, we selected 6 transverse sections through the tumor for our ASL studies. Image acquisition was done at 8 TI times. For the first slice, minimum inversion time was 300 ms, and subsequent inversion times were increased by 250 ms. The labeling slab thickness was 130 mm, and it was positioned at the level of upper cervical region. The imaging parameters for the ASL sequence were as follows: TR/TE = 250/16 ms, flip angle = 40°, FOV = 240 × 240 cm, matrix = 68 × 68, slice thickness/gap = 6/0.6 mm, number of dynamics = 30. A total of 2880 images, including 1440 labeled and 1440 control images, were obtained. The total acquisition time was 4 min and 8 s. ASL images were transferred to an off-line workstation (Philips Extended MR workspace, R.2.6.3.2, 2009) and subtraction images and rCBF maps were obtained.

DSC-PI was performed after ASL image acquisition by a first passage contrast-enhanced T2-weighted single-shot gradient-echo echo-planar sequence. The parameters of the sequence were as follows: TR/TE = 1513/40 ms, flip angle = 75°, FOV = 224 × 224 mm, matrix = 96 × 95, slice thickness = 5 mm, slice gap = 0 mm, and total data acquisition time = 65 s. As a contrast material, 20 ml gadodiamide (Omniscan, Nycomed, Norway) was administered using an 18 ga IV catheter at a rate of 5 ml/s automatically (Spectris Solaris EP MR Injection System, Medrad) by the antecubital venous method. This was followed by 20 ml serum physiological liquid injection at nearly the same rate. After the perfusion MRI, contrast-enhanced T1-weighted 3D-TFE sequence was acquired.

2.3. Data processing

Image analysis was performed in Extended MR workspace (Version 2.6.3.2, 2009, Philips Medical Systems) with the special application tools “neuro perfusion” and “image algebra” for DSC-PI and ASL-PI, respectively. After evaluating the conventional MRI sequences, ASL and DSC images were evaluated and perfusion maps are created. Qualitative interpretation of lesions on perfusion images did not performed.

In ASL data processing, 48 subtraction images of the labeled and control images were obtained. A manually drawn elliptic region of interest (ROI) was placed on the solid and brightest portion of tumor seen in subtraction images, which was assumed as having high perfusion. The signal intensity of the lesion was normalized with the symmetrical region on the contralateral normal hemisphere (rSI). A program was written in MATLAB (The Mathworks Inc., Natick, MA) for calculating the absolute cerebral blood flow from ASL images. First, thirty dynamics of each slice were averaged to increase SNR. Brain tissue was masked from the control images for each slice. Main magnetization (M0) was estimated for each pixel of the masked images using the T1 relaxation equation at different phases of control images using T1 value of blood (1.664 s). Thereafter, cerebral blood flow was calculated by taking into account the arterial blood flow [9]. The inversion efficiency (α) was used as 0.95, T1 of tissue was used as 1.3 s, and the blood tissue water partition coefficient was taken as 0.9 for the whole brain.

For DSC data processing, arterial input function model was used. Middle cerebral artery (MCA) was selected as an arterial input for assessing CBF and CBV maps. For obtaining normalized values, the symmetrical region on the contralateral hemisphere was accepted as reference like in ASL data processing.

2.4. Statistical analysis

Five perfusion MRI parameters, which were rCBV and rCBF obtained from DSC-PI and CBF, rCBF, and rSI values obtained from ASL were evaluated. The capability of these perfusion values and ratios about differentiating low and high-grade gliomas was investigated with Mann-Whitney ranksum test. Bonferroni multiple comparison correction was used, and a p value of less than 0.01 was considered as significant. The correlation between perfusion parameters obtained with DSC and ASL was assessed using Spearman correlation analysis.

Receiver operating characteristic curve analysis was used to evaluate the association between the perfusion values and the